NOVEMBER 22, 1941

# THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, CHEMISTRY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6169 LONDON: SATURDAY, NOVEMBER 22, 1941 CCXLI

## CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

**ORIGINAL ARTICLES**

The Common Sulphonamides: Nomenclature, Structure and Uses. Sulphanilamide and its Derivatives — Chemotherapy Inside the Bowel —Other Sulphur Compounds. DENNIS G. ARDLEY, M.P.S. ..... 625

Active Immunisation Against Tetanus. Immunisation with Two Doses of Toxoid—Effect of a Third Dose. D. G. EVANS, PH.D. ..... 628

Placental Blood in the Treatment of Amenorrhœa. J. HALBRECHT, M.D. (*illus.*) ..... 630

Meningococcal Infection. Majors R. C. DICKSON, M.D., N. E. MCKINNON, M.B.; Captains D. MAGNER, M.D., N. B. MCGILLIVRAY, M.D. ..... 631

Paradoxical Cerebral Embolism, with Recovery. ALAN GRAHAM PORTER, M.B. ..... 634

Isoagglutinin Changes after Transfusion of Incompatible Blood and Serum. P. L. MOLLISON, M.R.C.P.; I. MAUREEN YOUNG, B.SC. (*with charts*) ..... 635

Stab Wounds of the Heart and Pericardium: Four Cases with Three Recoveries. THEODORE SCHRIRE, F.R.C.S. ..... 638

Home Visiting of Defaulting Venereal-disease Patients. J. L. BURN, M.D. ..... 655

**REVIEWS OF BOOKS**

Lymphatics, Lymph and Lymphoid Tissue: Their Physiological and Clinical Significance. Prof. C. K. Drinker, M.D., J. M. Yoffey, F.R.C.S. ..... 640

Sick Children. Donald Paterson, F.R.C.P. ..... 640

Textbook of the Practice of Medicine. Editor: Frederick W. Price, F.R.C.P. ..... 640

Second Yearbook of Research and Statistical Methodology. Editor: O. K. Buros ..... 640

**SPECIAL ARTICLES**

Injuries and Diseases of War: A National Pathological Collection ..... 647

Medical War Relief Fund .. 647

Output and the Worker: "Apply existing Knowledge" ..... 648

Infectious Disease in England and Wales ..... 648

**IN ENGLAND NOW**

A Running Commentary by Peripatetic Correspondents ..... 649

**PARLIAMENT**

On the Floor of the House 650

**LEADING ARTICLES**

REST FOR INFLAMED TISSUES ..... 641

THE HAY-BOX REDIVIVUS 642

IMMUNITY TO TETANUS .... 643

**ANNOTATIONS**

A Ministry of Medical Services ..... 644

Surgery for Syringomyelia 644

Man-power of the Disabled 644

Operation for Hypertension 645

Renal Complications of Chemotherapy ..... 646

Radiography of the Heart 646

**LETTERS TO THE EDITOR**

Working Hours ..... 652

Pneumococcal Meningitis (Dr. Thomas Anderson). 652

When to Tie the Cord (Dr. A. E. Chisholm, F.R.C.O.G.) ..... 652

What's in the Loaf? (Dr. S. W. Swindells) ..... 653

Perinæal Suture under Local Anæsthesia (Prof. F. J. Browne, F.R.C.O.G.) ..... 653

Student and Screen (Dr. Ronald MacKeith) ..... 653

Disposal of Stillborn Children ..... 654

**OBITUARY**

Hugh Moreland McCrea, M.D. (*with portrait*) ..... 651

Millice Culpin, L.R.C.P.E. .. 651

**MEDICAL NEWS**

Royal College of Surgeons of England ..... 654

Society of Apothecaries of London ..... 654

University of Wales ..... 654

University of Sheffield .... 654

Royal Society of Medicine 654

Vitamins for Babies ..... 654

Medical Society of London 655

Medico-Legal Society ..... 655

International Hospital Association ..... 655

War Wounds Committee in Scotland ..... 655

Domestic Staff in Hospitals 655

Biochemical Society ..... 655

Socialist Medical Association ..... 655

Control of Scabies ..... 655

Anglo-Soviet Medical Committee ..... 655

Royal Medico-Psychological Association ..... 655

Prisoner of War ..... 654

Calls to the Bar ..... 655

Reeve to the L.C.C. ..... 656

Training the Luftwaffe Doctor ..... 651

Scobenzol (Boots) ..... 635

Siccolam (B.D.H.) ..... 635

Preparation of Plaster Casts 650

Appointments — Births, Marriages and Deaths ... 654

***A new edition***

**EXTRA PHARMACOPŒIA (MARTINDALE)**

*Volume I. 22nd Edition. 1289 pages. Price 27/6, postage 6d. extra. Remittance with order.*

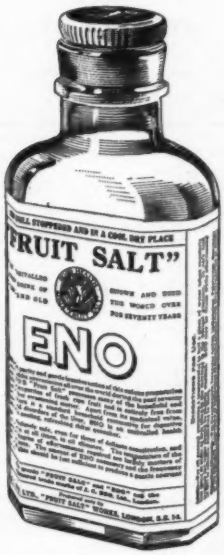
***• Points of interest***

• Detailed information on every worth-while development in therapeutics evolved during recent years. • Over two thousand new abstracts selected from the literature of the past four years. • Descriptions of thousands of proprietary medicines used in prescribing and dispensing. • An indispensable aid to memory in selecting suitable alternatives for drugs and chemicals in short supply. • A new Therapeutic Index the entries in which are keyed by page references to the text.

*"The book is a compendium of information otherwise only obtainable, in many instances, by reference to numerous text-books and by arduous searching through the scientific literature."*—LANCET.

**THE PHARMACEUTICAL PRESS, 17, Bloomsbury Square, London, W.C.1**

# THE IDEAL LAXATIVE FOR PROLONGED USE




Certain characteristics have won for ENO'S "FRUIT SALT" a very high place in professional regard. Few simple medicines are presented in so attractive a form, and for patients obliged to maintain prolonged use of a laxative ENO'S "FRUIT SALT" provides a highly satisfactory answer.

By the natural process of osmotic diffusion ENO'S "FRUIT SALT" creates healthy intestinal conditions, from which follow gentle regular and complete bowel evacuations.

The morning dose of ENO'S "FRUIT SALT" is universally regarded in a singularly favourable light. It is refreshing, exceedingly pleasant to drink. It is non-irritating, non-toxic, non-habit forming and free from sweetening agent. Diabetic patients may take it in perfect safety and, owing to the absence of sulphates, ENO'S "FRUIT SALT" may be confidently prescribed for patients receiving sulphonamide treatment.

*Further information available on request*

**J. C. ENO LTD.,** *MEDICAL DEPARTMENT,* **GREAT WEST RD., BRENTFORD, MIDDLESEX**

*The Standard Antacid for Routine Use*

For the past generation 'MILK OF MAGNESIA' has been accepted as the antacid of proved efficacy. Its routine use is markedly beneficial in combating hyperacidity. Possesses mild laxative properties.

CHARLES H. PHILLIPS CHEMICAL CO.
Successors
PROPRIETARY AGENCIES Ltd.
179, Acton Vale, London, W.3

# 'MILK OF MAGNESIA'
REGD.

*'Milk of Magnesia' is the Registered Trade Mark of Phillips' preparation of magnesia.*

MISSING PAGES ARE ADVERTISING PAGES.
THIS IS THE BEST COPY AVAILABLE FOR
PHOTOGRAPHY.

# ORIGINAL ARTICLES

## THE COMMON SULPHONAMIDES
### NOMENCLATURE, STRUCTURE AND USES

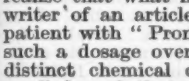
DENNIS G. ARDLEY, M.P.S.

WITH the inevitable increase in the number of compounds introduced into clinical practice for the chemotherapy of bacterial infections the need of an accurate and uniform nomenclature becomes urgent. Few modern British books on general medicine or the specialties make any attempt to achieve accuracy in the names used for these compounds, and the medical journals and encyclopædias tend to pander to the whims of their contributors instead of exerting strict control over the names employed. As a consequence, for example, all the names which happen to have been employed for the same chemical compound by various contributors to a textbook may appear in different parts of the index. Abstracts of articles from foreign journals often use for drugs names which are unfamiliar to readers in this country and in this way the chief point of the abstract may be lost. Conversely, proprietary names and erroneous nomenclature in English articles duly find their way into foreign abstracts to the mystification of readers. The practitioner who writes a prescription for "sulphonamide," ½ gramme tablets, or the surgeon who orders a wound to be dressed with sulphonamide powder, does not realise that what he has ordered is meaningless. The writer of an article who describes the treatment of a patient with "Prontosil" given by mouth in such and such a dosage overlooks the fact that there are three distinct chemical compounds to which this name is applied, and that all are given by mouth. The limit appears to have been reached by the author of an article on the use of various sulphonamide compounds who calmly announced at the outset that a particular brand name for sulphanilamide would be used to describe all the different compounds employed! It therefore seems opportune to suggest a few rules for general guidance. First, about dosage. The common practice of describing oral dosage in terms of number of tablets or volume of a suspension is inadvisable. A discussion once arose concerning an article on the treatment of gonorrhœa in which the dosage of sulphanilamide employed was in dispute until it was realised that the author was expressing dosage in drachms of a proprietary suspension. Dosage should always be expressed in terms of the active ingredient.

Most of the sulphonamides in common use have three kinds of name—a chemical name often occupying a line of print, a scientific synonym or pet-name, being the chemical name in a shortened form, and a various number of trade names. The synonym is the one intended for use in scientific articles, but unfortunately not all the compounds have one, and in some cases the trade name is at present unavoidable. Whenever possible only the full chemical name or its shortened form should be used, though it may sometimes be convenient to indicate once in an article which particular brand was employed.

#### SULPHANILAMIDE AND ITS EARLIER DERIVATIVES

Para-aminobenzenesulphonamide or para-aminophenylsulphonamide is the simplest and most widely used of these drugs, and being the amide of sulphanilic acid the name now commonly adopted of sulphanilamide is at once both accurate and brief, and the employment of proprietary names for this compound in medical literature is inexcusable. Of the forty or so trade names indicating proprietary brands of this compound the commonest ones in this country are Colsulanyde, Prontosil album and Streptocide, and sometimes the non-proprietary designations sulphonamide-P or P.A.B.S. are used. A proprietary brand much used in America is known as Prontylin. Some clinicians still do not realise that these names all stand for the same substance, and it is not unusual to hear of a patient's treatment being changed from one make of sulphanilamide to another, because he did not respond to the brand first ordered. Many other proprietary names for sulphanilamide, less commonly used than the four already given, are encountered, chiefly in foreign medical literature. In table I will be found 42 trade names for sulphanilamide, among which collectors may find choice and rare specimens. In the case of a few trade names encountered in foreign medical journals there has been no clue to the composition of the drug, or the composition has been variously described in different articles so that it has been impossible to be certain what the compound was. Sulphanilamide was included in the Fourth Addendum to the B.P. 1932.



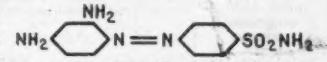
Sulphanilamide

TABLE I—PROPRIETARY NAMES FOR SULPHANILAMIDE

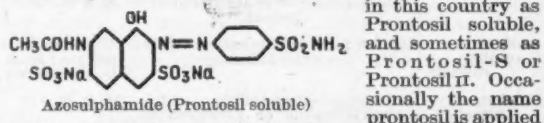
| | | | |
|---|---|---|---|
| Albosal | Gombardol | Septamide album | Streptocom |
| Ambesid | Lysococcine | Septanilam | Strepton |
| Antistrept | Neococcyl | Septinal | Streptozone |
| Astreptine | Orgaseptine | Septoplix | Sulfamidyl |
| Bacteramide | Prontosil album | Stopton album | Sulfana |
| Bactesid | Prontylin | Stramid | Sulfanil |
| Cepticide | Pronzin album | Strepamide | Sulphanalone |
| Colsulanyde | Proseptine | Streptamid | Supron |
| Deseptyl | Proseptol | Streptazol | Therapol |
| Ergaseptine | Pysoccine | Streptocide | |
| Erysipan | Rubiazol-A | Streptoclase | |

The simplest and most convenient classification of other sulphonamide drugs is to regard them as derivatives of sulphanilamide and as falling into two groups according to whether substitution takes place in the amino ($NH_2$) or in the amide ($SO_2NH_2$) portion of the molecule (table II). All the earlier compounds belong to the first class and are split up with release of sulphanilamide in the body. The more active substances introduced subsequently, such as sulphapyridine and sulphathiazole, fall into the second category, and these compounds do not depend for their action on the production of sulphanilamide.

The first compound to be employed was sulphonamido-chrysoïdin, which is 4′-sulphonamido-2 : 4-diaminoazobenzene, introduced into commerce under the name prontosil after having been called Streptozon. The name prontosil strictly refers, therefore, to this azo dyestuff but most English clinicians use it to designate sulphanilamide. If the word is used at all it should never be employed without qualification, so that there is no doubt as to meaning. Sulphonamido-crysoïdin is also known as Prontosil flavum or Prontosil rubrum. A less common trade name is Pronzin rubrum. A more soluble compound was later introduced for parenteral administration, which consists of a solution of the disodium salt of 4′-sulphonamidobenzene-2-azo-1-hydroxy-7-acetylaminonaphthalene-3 : 6-disulphonic acid, usually known in this country as Prontosil soluble, and sometimes as Prontosil-S or Prontosil II. Occasionally the name prontosil is applied to this compound instead of to sulphonamido-chrysoïdin, and in America, where it is given by mouth in place of the latter, it is known under the proprietary name of Neoprontosil, the "descriptive non-proprietary name" proposed for this substance by the Council on Pharmacy and Chemistry of the American Medical Association being azosulfamide. The name streptozon has been given to both prontosil rubrum and prontosil soluble, the latter having sometimes been distinguished as Streptozon II or S, and curiously enough the designation Prontosil red is sometimes used for prontosil soluble rather than prontosil rubrum. The Rubiazols include the French equivalents of the German azo sulphonamides and rival them in confused terminology. It is, however, sufficient to remember that in this country the name rubiazol is applied to a compound which differs from sulphonamido-chrysoïdin in containing a carboxyl (COOH) grouping, and hence is conveniently described as carboxysulphonamido-chrysoïdin.



Sulphonamido-chrysoïdin



Azosulphamide (Prontosil soluble)

In common with most other compounds of the first group in which substitution takes place in the amino

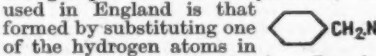
TABLE II

SULPHANILAMIDE DERIVATIVES, AND SULPHONES

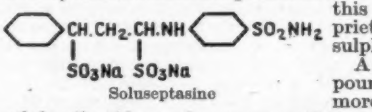
| Synonym or abbreviated chemical name | Full chemical name | Proprietary names |
|---|---|---|
| **SULPHANILAMIDE DERIVATIVES, FIRST CLASS** | | |
| Sulphonamido-chrysoidin | 4'-sulphonamido-2 : 4-diaminoazobenzene | Prontosil (flavum or rubrum); Streptozon; Pronzin rubrum |
| Azosulphamide | Disodium 4'-sulphonamidobenzene-2-azo-1-hydroxy-7-acetyl-amino-naphthalene-3 : 6-disulphonate | Prontosil soluble; Neoprontosil |
| Carboxysulphonamido-chrysoidin | 4'-sulphonamido-2 : 4-diamino-6-carboxyazobenzene | Rubiazol |
| Benzylsulphanilamide | *p*-benzylaminobenzenesulphonamide | Proseptasine (M. & B. 125); Septazine; 46 R.P. |
| Sodium succinyl sulphanilamide | Sodium *p*-succinylaminobenzenesulphonamide | Ambesid soluble; Septinal soluble |
| None | Disodium-*p*-(γ-phenyl-propylamino)-benzene-sulphonamide-α-γ-disulphonate | Soluseptasine (M. & B. 137); Soluseptazine; 40 R.P. |
| ,, | Sulphanilamide lactoside sodium formaldehydesulphoxylate | Sulphanilamide L.S.F. |
| ,, | Sodium-4-sulphonamido-phenylaminoethane α sulphonate | Sulphonamide E.O.S. |
| **SULPHANILAMIDE DERIVATIVES, SECOND CLASS** | | |
| Sulphanilyl-dimethyl-sulphanilamide | *p*-aminobenzenesulphonamido-benzenesulphondimethylamide | Uleron; Uliron; Ulirone; D.B. 90; D.B. 373; Diseptal A |
| Sulphanilyl-monomethyl-sulphanilamide | *p*-aminobenzenesulphonamido-benzenesulphonmonomethylamide | Neo-uliron; Diseptal B |
| Sulphanilyl-sulphanilamide | *p*-aminobenzenesulphonamido-benzenesulphonamide | Diseptal C; Disulon |
| Sulphapyridine | 2-(*p*-aminobenzenesulphonamido) pyridine or 2-sulphanilylamino-pyridine | Dagenan; M. & B. 693; Eubasinium; Septipulmon; Pyriamid |
| Sodium sulphapyridine | Sodium 2-(*p*-aminobenzenesulphonamido) pyridine | Dagenan sodium; M. & B. 693 soluble |
| Sulphathiazole | 2-(*p*-aminobenzenesulphonamido) thiazole or 2-sulphanilylamino-thiazole | Thiazamide; M. & B. 760. |
| Sodium sulphathiazole | Sodium 2-(*p*-aminobenzenesulphonamido) thiazole | Thiazamide sodium; M. & B. 760 soluble |
| Sulphamethyl-thiazole | 2-(*p*-aminobenzenesulphonamido)-4-methylthiazole or 2-sulphanilyl-amino-4-methylthiazole | M. & B. 838 |
| Sulphadiazine | 2-(*p*-aminobenzenesulphonamido) pyrimidine or 2-sulphanilyl-aminopyrimidine | .. |
| Sulphacetamide | *p*-aminobenzenesulphonacetamide | Albucid; Sulamyd |
| Sodium sulphacetamide | Sodium *p*-aminobenzenesulphonacetamide | Albucid soluble; Sulamyd soluble |
| Sulphaguanidine | *p*-amino-N-guanylbenzenesulphonamide or sulphanilylguanidine | .. |
| **SULPHONES** | | |
| None | Diacetyl-4 : 4'-diamino-diphenyl-sulphone | Rodilone (1399 F.) |
| ,, | 4-: 4-diaminodiphenylglucoside | .. |
| ,, | Sodium *p.p'*-diamino-diphenyl-sulphone-$N_1$-$N^1$-di-dextrose sulphonate | Promin |

radical of sulphanilamide, these substances owe their activity mainly to the release of sulphanilamide itself in the body tissues, the coloured compounds being split at the azo linkage. Endeavours have been made to show that the azo linkage per se may play a rôle in their action, but all the important recent advances concern colourless compounds, and the dye-stuffs cannot but be regarded as being chiefly of historic interest.

Of the sulphanilamide derivatives belonging to the first group which are not dye-stuffs, the most commonly used in England is that formed by substituting one of the hydrogen atoms in the amino group by a benzyl group. This compound is para-benzylaminobenzenesulphonamide or benzyl sulphanilamide. It is known in England as Proseptasine or M. & B. 125, and in France as Septazine or 46 R.P. The drug is soluble in water only to the extent of about 1 in 25,000, compared to sulphanilamide which has a solubility of about 1 in 100. The sodium salt of the corresponding succinyl derivative of sulphanilamide—sodium para-succinylaminobenzenesulphonamide or sodium succinyl sulphanilamide—has been issued for parenteral administration under the name Ambesid soluble. There is also a product Ambesid, and it might reasonably be expected that this would be succinylaminobenzenesulphonamide itself, but in fact this is another proprietary name for sulphanilamide.



Benzylsulphanilamide



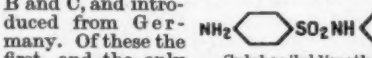
Soluseptasine

A widely used compound which is much more soluble than sulphanilamide and consequently more suitable for parenteral administration is Soluseptasine or M. & B. 137, known in France as Soluseptazine or 40 R.P. It is disodium-*p*-(γ-phenyl-propylamino)-benzene-sulphonamide-α-γ-disulphonate, the sodium sulphonate part of the molecule being the solubilising groups. No convenient non-proprietary designation for soluseptasine has come into use.

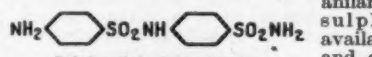
A soluble sulphanilamide derivative for parenteral administration, and one having a high sulphanilamide content, has recently been placed on the market under the name sulphanilamide L.S.F. It is described as sulphanilamide lactoside sodium formaldehydesulphoxylate. Reference has also been made to a compound called Sulphonamide E.O.S. and described as the sodium salt of the ethylsulphonic acid of sulphanilamide. It therefore appears to be sodium 4-sulphonamidophenylaminoethane α sulphonate. It has been tried clinically in cattle and man. Mutch (1941) has described some investigations on its pharmacology and activity and has given details of its use in 34 cases of cerebrospinal fever.

### LATER DERIVATIVES

The first drugs of the second class were three disulphanilamide compounds, known originally as Diseptal A, B and C, and introduced from Germany. Of these the first, and the only one to come into use in England, is known as Diseptal or Uleron. It is also called Uliron, Ulirone, D.B. 90 or D.B. 373, and is para-aminobenzene sulphonamido-benzenesulphondimethylamide or sulphanilyldimethylsulphanilamide. Diseptal B is the corresponding monomethyl derivative, and is now referred to in German medical literature as Neo-Uliron. Diseptal C contains no methyl groups, being sulphanilylsulphanilamide. Sulphanilylsulphanilamide is available in America and on the Continent under the name Disulon, where it is used in the treatment of gonorrhœa. It is also known as "disulphanilamide," a name which, unfortunately, has also been used for the dimethyl derivative (uleron). Claims that uleron is valuable for the treatment of gonococcal, staphylococcal and anaerobic infections have not been substantiated, and the subsequent use of sulphapyridine for the treatment of gonorrhœa and the activity of sulphathiazole in staphylococcal infections have led to its falling into disuse. In

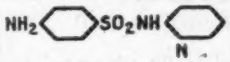


Sulphanilyldimethylsulphanilamide (Uleron)



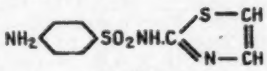
Sulphanilylsulphanilamide

common with most other derivatives of the second class uleron is not broken down with the release of sulphanilamide but is eliminated partly unchanged and partly in a conjugated form.



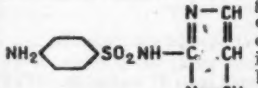
Sulphapyridine

An event of outstanding importance in chemotherapy was the introduction of the compound derived from sulphanilamide by substitution of one hydrogen atom in the amide portion of the molecule by a basic pyridine group, giving 2-(*p*-aminobenzenesulphonamido) pyridine. This was first known as T. 693, later introduced as M. & B. 693 and subsequently called Dagenan, a mutation on an Essex place name. To a non-chemist sulphanilylaminopyridine should not be too long to remember but the Americans christened the compound sulphapyridine, which name, although not accurately descriptive chemically, has been generally accepted. Sulphapyridine proved to have a much higher degree of activity than sulphanilamide, thereby extending the range of chemotherapy far beyond infections by sulphonamide-susceptible strains of streptococci. Pneumococcal infections were brought under control, a more potent weapon against gonococcal, meningococcal and gas-gangrene infections provided, and the effective chemotherapy of plague and staphylococcal infections brought nearer. A calcium compound of sulphapyridine has been placed on the market in Germany under the trade name Orsulon. It is issued in tablets for oral administration in the treatment of pneumococcal and other infections. In Stockholm a compound of sulphapyridine and salicylic acid, known as salicylazosulphapyridin, and marketed as Salazopyrin, has been used with success in rheumatoid arthritis and ulcerative colitis.



Sulphathiazole

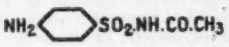
An even more active compound than sulphapyridine is the corresponding thiazole derivative 2-(*p*-aminobenzenesulphonamido) thiazole or 2-sulphanilylaminothiazole, usually called sulphathiazole, and also known in England as Thiazamide or M. & B. 760, in Switzerland as Cibazol or Ciba 3714, and in France as R.P. 2090. It has proved its value in the treatment of infections with *Staphylococcus aureus*, some of the clostridia, *Pasteurella pestis*, and various organisms found in urinary-tract infections, including *Streptococcus fæcalis*. Various compounds obtained by replacing one of the hydrogen atoms in the thiazole ring have been tried in therapeutics, and of these the name sulphamethylthiazole indicates the 4-methyl derivative—namely, 2-(*p*-aminobenzenesulphonamido)-4-methylthiazole, or 2-sulphanilyl-amino-4-methylthiazole (M. & B. 838). Owing to the danger of peripheral neuropathy from the use of these derivatives (cf. uleron which also contains methyl groups), and their greater liability to deposit crystals in the urinary tract compared to sulphathiazole itself, little more is likely to be heard of them.



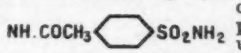
Sulphadiazine

Another heterocyclic derivative of sulphanilamide, the pyrimidine analogue of sulphapyridine, has recently been introduced in America; this is 2-(*p*-aminobenzenesulphonamido) pyrimidine or 2-sulphanilyl-aminopyrimidine. Sulphadiazine, as it is called, appears from the preliminary studies of American workers such as those of Finland, Strauss, and Peterson (1941) and of Long (1941) and his associates at Johns Hopkins Hospital to have about the same degree of activity as sulphathiazole and sulphapyridine on pneumococci and meningococci, to have an activity on *Staph. aureus*, and to have a high degree of activity on *Klebsiella pneumoniæ* (Friedländer's pneumobacillus). It has been tried in pneumococcal pneumonia, cerebrospinal fever, staphylococcal, streptococcal, gonococcal and other infections but the data at present available concerning its activity, toxicity, absorption, distribution and elimination are inadequate to predict its ultimate place in chemotherapy.

Sulphapyridine and sulphathiazole being of low solubility in water are unsuitable for parenteral administration in solution, for which purpose their sodium salts are employed. The latter being compounds of weak acids with a strong base yield solutions which are highly alkaline. If one of the amide hydrogen atoms of sulphanilamide is replaced by an acetyl radical the compound *p*-aminobenzenesulphonacetamide is formed, which is known as sulphacetamide and was introduced under the proprietary name Albucid. It has been advocated for use in gonorrhœa, for which purpose it is less effective than sulphapyridine but rather strikingly free from toxic effects, owing probably to its low solubility and consequent poor absorption from the alimentary tract. Its sodium salt differs from the sodium salts of sulphathiazole and sulphapyridine in not yielding a highly alkaline solution. Sodium sulphacetamide is issued as Albucid soluble or Sulphacetamide soluble. It is employed intramuscularly and as a 30% solution for intravenous injection, and a 2·5% solution has been advocated for application to the eyes in the prophylaxis of bacterial infection following injury by vesicant war gases. Albucid and albucid soluble have been placed on the market in Canada under the names Sulamyd and Sulamyd soluble. Sulphacetamide differs from the acetyl derivative of sulphanilamide, into which the latter is partly converted in the body, since in sulphacetamide it is a hydrogen of the amide group which is replaced by the acetyl radical, whereas with acetyl sulphanilamide substitution takes place in the amino group. Analogous conjugation takes place with sulphapyridine, sulphathiazole, sulphadiazine and a number of other sulphonamide drugs. Unlike these compounds sulphacetamide appears to be partly broken down in the body to sulphanilamide.



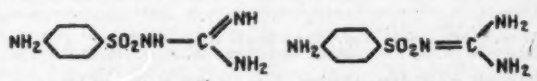
Sulphacetamide



Acetyl sulphanilamide

### CHEMOTHERAPY INSIDE THE BOWEL

The absorption of a sulphonamide from the alimentary tract or from a wound chiefly depends on its solubility in water at body temperature. Thus the solubility and absorbability of sulphanilamide, sulphathiazole and sulphapyridine decrease in that order. Other factors, however, have an influence on degree and rate of absorption, and some compounds, much more soluble than sulphapyridine or sulphathiazole, have a low degree of gastro-intestinal absorption. The idea arose, therefore, of using a sulphonamide which is bacteriostatically active, fairly water-soluble and of low absorbability to combat infections which are largely confined to the alimentary canal. Marshall, Bratton, White and Litchfield (1940), who studied various compounds from this point of view, found that sodium sulphanilyl sulphanilate, $N^1$-(2-hydroxyethyl) sulphapyridine, $N^1$-diglycosulphapyridine and sulphanilylguanidine fulfilled the requirements of water-solubility and limited absorption from the intestine. Since sulphanilylguanidine appeared to be the most active of these compounds against a number of pathogens it was selected for pharmacological and therapeutic investigation. (It may be recalled that sodium sulphanilyl sulphanilate once achieved a short-lived but world-wide interest for a supposed activity in virus infections.) Sulphanilylguanidine is *p*-amino-N-guanylbenzenesulphonamide. Marshall and his colleagues suggest that the formulæ may both be considered correct for the compound as they are probably resonance isomers, easily transformed one into the other.



α-sulphanilylguanidine β-sulphanilylguanidine

Sulphaguanidine

The blood levels reached after the administration of sulphanilylguanidine are low as a consequence of its limited absorption, and the concentration in the gastro-intestinal tract is correspondingly high. It is suggested for trial in bacterial infections which are chiefly localised in the intestines, such as bacillary dysentery, cholera and the early stages of the enteric fevers, and for reducing the hazards of intestinal surgery. In acute bacillary dysentery it will have to be established that sulphanilylguanidine has advantages over sulphathiazole and sulphapyridine, those "veritable Excaliburs, with which dysentery apparently may be vanquished without fail"

(Ravenel and Smith (1941)). Other sulphonamides have proved inactive on *Vibrion choleræ* at ordinary therapeutic concentrations but Marshall and others have found sulphanilylguanidine bactericidal in vitro in a concentration of 200 mg. per 100 c.cm., so that at the high levels reached in the gastro-intestinal tract it is possible that the administration of this compound may be of benefit in cholera. Its use in intestinal infections bears some analogy with the use of sulphonamides in infections of the urinary tract, where the concentration in the urine is, of course, enormously greater than in the blood and tissues.

Various sulphonamides have given unquestionable benefit in cases of ulcerative colitis, although the mechanism of the effect must necessarily remain obscure while the ætiology of this condition is unknown, and a few experiences in the use of sulphanilylguanidine in ulcerative colitis are encouraging. The drug is being known as sulphaguanidine, by analogy with sulphapyridine and sulphathiazole.

### OTHER SULPHUR COMPOUNDS

Not all the sulphur compounds which are active antibacterial agents are sulphonamides; a number are sulphones, sulphoxides and sulphides. The sulphones (table II), which have been investigated experimentally as well as clinically, may be regarded as derivatives of 4 : 4′-diaminodiphenylsulphone. This substance has proved excessively toxic to mice but not to some other laboratory animals, and its toxicity probably precludes its clinical employment in man. McEwen, Pizer and Paterson (1941) have reported the rather unexpected finding that the compound is of relatively low toxicity for cattle, producing no toxic effects in therapeutic doses. The di-acetyl derivative of 4 : 4′-diaminodiphenylsulphone is of low toxicity and has been used in France for the treatment of gonorrhœa under the proprietary name Rodilone (1399 F.). The glucoside of 4 : 4′-diamino-diphenylsulphone has been studied for its activity in experimental bacterial and virus infections, and has been used clinically in the treatment of cerebrospinal fever, trachoma and lymphogranuloma inguinale. A compound known as Promin and described as the sodium salt of *p.p′*-diamino-diphenyl-sulphone-N,-N¹-didextrose sulphonate has been tried in artificially induced animal infections with various coccal and bacillary organisms, and used clinically by mouth and intravenously. This drug has been found to possess a retarding influence in experimental tuberculous infections of guineapigs apparently greater than that conferred by sulphonamides. At present, however, the effective chemotherapy of clinical tuberculous infections remains, with that of brucellosis, and the introduction of virucidal agents, probable achievements of the future. Despite the number of compounds in clinical use and the far greater number which have been studied experimentally, the tremendous strides made during the past few years constitute but the beginning, howbeit a highly successful one, of a new era in therapeutics.

### REFERENCES

Finland, M., Strauss, S. and Peterson, O. L. (1941) *J. Amer. med. Ass.* **116**, 2641.
Long, P. H. (1941) *Bull. Johns Hopk. Hosp.* **68**, 350.
McEwen, A. D., Pizer, N. H. and Paterson, J. D. (1941) *Vet. Rec.* **53**, 429.
Marshall, E. K. Jun., Bratton, A. C., White, H. J. and Litchfield, J. T. Jun. (1940) *Bull. Johns Hopk. Hosp.* **67**, 163.
Mutch, N. (1941) *Brit. med. J.* **2**, 503.
Ravenel, S. F. and Smith, D. L. (1941) *Sth med. J.* **34**, 504.

---

Two footnotes from "The New Chemotherapy in Puerperal Infections," by G. F. Gibberd (*Guy's Hosp. Gaz.* Nov. 15, 1941, p. 290).

Note for those who think that curative medicine began with the discovery of sulphanilamide. N.B.—Prior to 1936 more than half of the patients suffering from hæmolytic streptococcal septicæmia in the puerperium did, in fact, recover.

Note for those who believe in the maxim "when in doubt give sulphanilamide." N.B.—One of the deaths in the 1936–39 group occurred in a patient whose infection was proved at post-mortem examination to have been confined entirely to the birth-canal. She died from agranulocytosis, not from hæmolytic streptococcal infection. She died from sulphanilamide. She died from treatment.

# ACTIVE IMMUNISATION AGAINST TETANUS

D. G. EVANS, PH.D. MANC.
(*National Institute for Medical Research*)

Ramon and Zoeller (1927) originally advocated the use of tetanus toxoid for the active immunisation of man against tetanus infection, and since then immunisation has been practised extensively in many countries, especially since the outbreak of the present war. The type of antigen to be used, the dose to be administered, the number of doses to be given and the interval between the doses have been the subject of much discussion and research. The methods by which active immunisation with toxoid is effected vary in different countries. On the Continent it is usual to administer three doses of toxoid at relatively short intervals, but Boyd (1938) showed that equally good results were obtained by giving two doses, each of 1 c.cm. at an interval of not less than 6 weeks, and this practice is followed in England, Canada and several other countries. Boyd pointed out that 6 weeks may not be the optimum interval and suggested that wider spacing of the doses might achieve better results. His main observations have been confirmed by many workers, and Marvell and Parish (1940) have shown that when the doses are injected at an interval greater than 6 weeks a larger quantity of antitoxin is produced. Maclean and Holt (1940) have recently shown that a good response follows the injection of two doses of toxoid given at an interval of 4 weeks, and that when the toxoid is combined with T.A.B. vaccine the response, as judged by the antitoxin formed, is even better. They consider that it is unnecessary to prolong the interval from 4 to 6 weeks when the toxoid is combined with T.A.B. vaccine. From the administrative point of view there appears to be an advantage in employing two rather than three doses and there is a large amount of evidence and experience in support of the efficacy of two widely spaced doses. On the other hand, the administration of three doses of toxoid, each of 1 c.cm., at an interval of 3 weeks between the doses is recommended for the immunisation of the military personnel of the United States of America (Bain 1941).

The procedure finally adopted will, no doubt, be based on the results of trials made in different ways. In July, 1940, active immunisation was offered to members of the staff of the National Institute for Medical Research, Hampstead. The method of immunisation was similar to that of Boyd, but the opportunity was taken (*a*) of investigating the effect of increasing the interval between the doses of toxoid to 9 weeks, (*b*) of determining the antitoxin content after a single injection of toxoid, as well as 4 and 10 months after the second injection, and (*c*) of investigating the effect of giving a third dose of toxoid 10 months after the second dose.

### IMMUNISATION WITH TWO DOSES OF TOXOID

Two doses of tetanus toxoid each of 1 c.cm. were injected at an interval of 9 weeks into 81 subjects. The toxoid was given subcutaneously into the left arm and blood samples taken on three occasions: (1) immediately before the first injection, (2) immediately before the second injection, and (3) 17 weeks after the second injection. A small group of 16 persons were bled for a fourth time 10 months after the second injection. The sera were tested for tetanus antitoxin and the results are given in table I.

Of the 81 sera tested before inoculation, no sample showed as much as 0·01 international unit per c.cm. Nine weeks after the first injection, 22 of the 53 persons whose sera were tested still had less than 0·01 unit of antitoxin, while the remainder had developed more than 0·01 unit and almost a fifth of the persons more than 0·1 unit.

These results suggest that some persons had some basal immunity, a condition which may exist without evidence for it always being shown by the presence of detectable amounts of circulating antitoxin. Even if a person has not developed any basal immunity previously, this is very effectively provided by the first injection of toxoid, since after the second injection all the 70 persons tested had developed more than 0·01 unit, all but 2 showed more than 0·02 unit and as many as 59 more

than 0·1 unit. It is to be noted that the values were recorded 17 weeks after the second injection, indicating that a high, and what is usually regarded as adequate, concentration of antitoxin had been maintained during this period. Moreover, the examination of the sera of 16 persons 10 months after the second injection showed that the level of the antitoxin had been substantially

TABLE I—TETANUS ANTITOXIN TITRES OF SERA FROM PERSONS BEFORE AND AFTER INOCULATION WITH TETANUS TOXOID

| Blood sample taken | No. of samples | No. of sera showing titre (I.U. per c.cm.) of | | | | | |
|---|---|---|---|---|---|---|---|
| | | less than 0·01 | more than 0·01 | more than 0·02 | more than 0·1 | more than 1 | more than 5 |
| Before first inoculation | 81 | 81 | 0 | 0 | 0 | 0 | 0 |
| 9 weeks after first inoculation .. | 53 | 22 | 31 | 22 | 10 | 0 | 0 |
| 17 weeks after second inoculation .. | 70 | 0 | 70 | 68 | 59 | 19 | 0 |
| 10 months after second inoculation .. | 16 | 0 | 16 | 16 | 14 | 0 | 0 |

maintained. Comparing the values in table II at 4 and 10 months after the second injection it is seen that, while those persons who had developed more than 1 unit of antitoxin showed some reduction in titre, in 9 of the cases the antitoxin content of the serum had remained unchanged.

It may be mentioned that 39 of the 81 subjects received, in the interval between the injections of the two doses of toxoid, two doses of T.A.B. vaccine, and 12 of these 39 also received an injection of influenza virus A vaccine within the same period. It cannot be assumed that these additional injections of other antigens were entirely without effect on the production of tetanus antitoxin, but the conclusion may safely be drawn that they did not interfere with the active immunisation against tetanus.

### EFFECT OF A THIRD DOSE

It is the practice in certain countries, particularly in the armed forces, to give a further injection of tetanus toxoid a year after the first immunisation has been completed (Ramon 1939, Bain 1940). In this series, the opportunity occurred of investigating the effect of a third injection of toxoid on the antitoxin content of 16 of the persons who had been successfully immunised by two injections 10 months previously. The effect of the third injection was studied by determining the antitoxin content (1) immediately before, (2) 5 days, (3) 12 days and (4) 30 days after the third inoculation.

TABLE II—TETANUS ANTITOXIN TITRES OF SERA FROM 16 PERSONS BEFORE AND AFTER A THIRD INOCULATION OF TETANUS TOXOID

| No. of serum | Antitoxin titre (I.U. per c.cm.) | | | | |
|---|---|---|---|---|---|
| | After 2nd inoculation | | After 3rd inoculation | | |
| | 4 months | 10 months | 5 days | 12 days | 30 days |
| 1 | 0·02–0·1 | 0·02–0·1 | 0·02–0·1 | 2–5 | 2–5 |
| 27 | 0·1–1 | 0·1–1 | 2–5 | 10–20 | 10–20 |
| 31 | 0·02–0·1 | 0·02–0·1 | 0·1–1 | 2–5 | 2–5 |
| 35 | 0·1–1 | 0·1–1 | 1–2 | 10–20 | 5–10 |
| 40 | 1–2 | 0·1–1 | 2–5 | 20–50 | 20–50 |
| 44 | 1–2 | 0·1–1 | 2–5 | 20–50 | 20–50 |
| 48 | 1–2 | 0·1–1 | 5–10 | 20–50 | 20–50 |
| 52 | 1–2 | 0·1–1 | 2–5 | 20–50 | 20–50 |
| 58 | 0·1–1 | 0·1–1 | 1–2 | 10–20 | 5–10 |
| 59 | 1–2 | 0·1–1 | 10–20 | 20–50 | 20–50 |
| 64 | 0·1–1 | 0·1–1 | 5–10 | 20–50 | 20–50 |
| 65 | 0·1–1 | 0·1–1 | 2–5 | 20–50 | 10–20 |
| 86 | 0·1–1 | 0·1–1 | 2–5 | 10–20 | 5–10 |
| 88 | 1–2 | 0·1–1 | 2–5 | 10–20 | 10–20 |
| 93 | 1–2 | 0·1–1 | 2–5 | 20–50 | 10–20 |
| 108 | 0·1–1 | 0·1–1 | 1–2 | 5–10 | 2–5 |

The results of these tests are given in tables II and III, and the values found 6 months earlier (that is 4 months after the second injection) are also included.

The response to the third injection, given 10 months after the second injection, was well marked. In every case but one there was an increase in the antitoxin produced 5 days after the injection, and this increase continued to the 12th day, when 8 samples contained more than twenty units, 5 more than ten units, 1 more than five units and 2 more than two units. This large increase was maintained, unchanged in 10 cases, for 30 days.

### DISCUSSION

The concentration of antitoxin in the circulating blood necessary to afford protection against tetanus is not precisely known. It may be that, as in the case of diphtheria, the actual concentration of antitoxin at the time of infection is not the sole factor in determining whether tetanus will develop when an actively immunised person is exposed to infection. The responsiveness of the immunising mechanism, established by the injection of toxoid, is considered by many authorities to be a factor of possibly equal importance. However, from the experience gained in the last war, there are good grounds for believing that a concentration of antitoxin of as little as 0·01 unit per c.cm. is adequate for preventing the onset of tetanus in wounded persons, and if this is so the results show, in agreement with those of others, that this concentration is produced and maintained for many months in persons who have received two spaced injections of toxoid.

The results also suggest a point which may be of practical administrative importance. Boyd showed that the interval between the two doses should not be less

TABLE III—SUMMARY OF FINDINGS IN TABLE II

| Blood sample taken | No. of sera showing titre (I.U. per c.cm.) of | | | | | | |
|---|---|---|---|---|---|---|---|
| | 0·02–0·1 | 0·1–1 | 1–2 | 2–5 | 5–10 | 10–20 | 20–50 |
| 4 months after second inoculation .. | 2 | 7 | 7 | 0 | 0 | 0 | 0 |
| 10 months after second inoculation .. | 2 | 14 | 0 | 0 | 0 | 0 | 0 |
| 5 days after third inoculation .. | 1 | 1 | 3 | 8 | 2 | 1 | 0 |
| 12 days after third inoculation .. | 0 | 0 | 0 | 2 | 1 | 5 | 8 |
| 30 days after third inoculation .. | 0 | 0 | 0 | 3 | 3 | 4 | 6 |

than 6 weeks, and these experiments have shown that the interval may be extended to 9 weeks. To extend the interval may sometimes be convenient; but in any case it is clear that the second dose may be deferred for several weeks at least without endangering the efficacy of the active immunisation.

A striking feature of a further injection of toxoid into actively immunised persons is the rapidity with which antitoxin is produced. There seems to be no record of the effect produced by absorption of the toxin in an actively immunised person infected with tetanus organisms; but, in so far as such a condition may be regarded as providing a secondary stimulus to the established immunising mechanism, these results suggest that the actively immunised person is provided, in his capacity to produce antitoxin rapidly in response to a specific stimulus, with an additional safeguard against the onset of tetanus. The administration of a further injection of toxoid a year or more after the first immunisation has much to recommend it. Although tetanus toxoid is remarkably certain in its action, there are, as judged by the antitoxin produced, some persons who respond better than others, and it is possible that in a larger series there might be some cases in which immunisation had apparently failed. In the case of tetanus there is, as yet, no simply applied test, like the Schick test in diphtheria, by which these failures can be discovered. If the procedure of giving a third injection after a year were generally applied those persons who did not become effectively immunised by the two earlier injections, as well as those in whom the antitoxin level had fallen, would be more certainly provided for, and the chance of an actively immunised person developing tetanus, which recent experience suggests to be very small (Perry 1940), would be still further reduced. The question whether the extra protection thus afforded would be offset by the additional trouble is one for administrative decision.

In view of the fact that actively immunised persons respond rapidly to a third injection by the production of antitoxin in large amounts, it has been suggested that persons wounded many months after immunisation need only be given toxoid and not antitoxin. Recent

advocates of such a procedure are Kestermann and Vogt (1940), and the U.S. War Department, in recently issued instructions governing the administration of tetanus toxoid and antitoxin to military personnel (Bain 1941), state that wounded persons who have been immunised are to be given tetanus toxoid, and those who have not been immunised are to be given antitoxin. There is, however, not sufficient evidence to support an assumption that the same dramatic increase in antitoxin would necessarily occur in persons in whom infection by other organisms had become established, or, as pointed out by Marvell and Parish (1940), in seriously wounded persons suffering from shock.

SUMMARY

Examination of the sera of 81 persons (age 15–60 years), before active immunisation against tetanus, showed that none contained as much as 0·01 international unit of tetanus antitoxin per c.cm.

Nine weeks after the first injection of tetanus toxoid, examination of the sera of 53 persons showed that in 31 cases the antitoxin content was more than 0·01 unit, but that 22 still contained less than 0·01 unit.

Seventeen weeks after the second injection of toxoid, given nine weeks after the first, all the 70 persons examined had more than 0·01 unit, 68 more than 0·02 unit, 59 more than 0·1 unit and 19 more than 1 unit.

The antitoxin level was substantially maintained for ten months after the second injection.

The administration of a third dose of tetanus toxoid ten months after the second injection to 16 of these persons was followed by a large and rapid increase in the antitoxin content of the serum, and the high level was maintained substantially unchanged for a month.

REFERENCES

Bain, J. A. (1941) *J. Amer. med. Ass.* **116**, 2857.
Boyd, J. S. K. (1938) *J. R. Army med. Cps*, **70**, 289.
Kestermann, E. and Vogt, K. E. (1940) *Klin. Wschr.* **19**, 1129.
Maclean, I. H. and Holt, L. B. (1940) *Lancet*, **2**, 581.
Marvell, D. M. and Parish, H. J. (1940) *Brit. med. J.* **2**, 891.
Perry, H. M. (1940) *Ibid*, **2**, 364.
Ramon, G. (1939) *Pr. méd.* **47**, 877.
— and Zoeller, C. (1927) *Ann. Inst. Pasteur*, **41**, 803.

# PLACENTAL BLOOD IN THE TREATMENT OF AMENORRHŒA

J. HALBRECHT, M.D.

DEPARTMENT OF GYNÆCOLOGY, BEILINSON HOSPITAL, PETAH TIQVA, PALESTINE

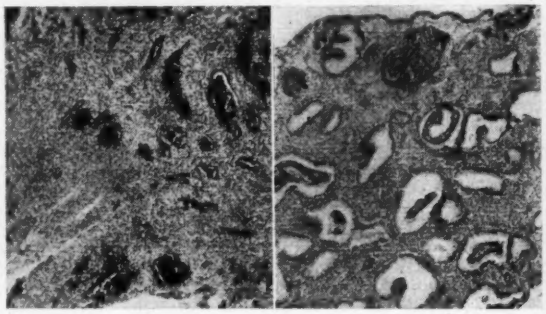
THE treatment of amenorrhœa and sterility with various gonadotropic hormones has been unsatisfactory up to now, owing to the fact that these hormones, though showing some effect on the ovaries of rodents, have none on the ovaries of women and monkeys. Recently positive results have been reported from the use of the serum of pregnant mares, but it is too early to give a conclusive verdict on its value.

It seems possible that gonadotropic preparations might fail because they contain an incomplete hormonal complex: they lack an activator which is present in the blood. This would explain the better results obtained with the serum of pregnant mares. I therefore decided to investigate the effect of placental blood. Vaginal bleeding and lactation in the newborn seem to indicate that placental blood is rich in hormones, though no exact laboratory estimate has yet been made of its hormonal content. If correctly obtained it causes no graver reactions than ordinary blood, and by using plasma I eliminated the danger of hæmolytic crises.

In order to determine whether placental blood really was active I gave injections of it to 34 amenorrhœic women, with the result that 18 menstruated within 5–35 days after the end of the course of treatment; in most of them menstruation began between the 15th and the 20th days. A further 3 patients menstruated on or after the 35th day. Of those I was able to follow up, 5 menstruated once only, 8 twice or more; the others were not traced. In the light of subsequent experience it seems likely that those who failed to menstruate may have received too little blood. At first I gave only three or four injections of blood. A few patients menstruated after receiving small quantities—a few drops—but others required larger amounts.

In 11 cases the effect of placental blood, or plasma, on the uterine mucosa was determined by histological examination before and after treatment.

*Method.*—Before treatment I dilated the cervix up to Hegar 5–6, curetted lightly with the finest curette, and examined the endometrium histologically. Treatment by placental blood or plasma was begun immediately afterwards. Each patient received 5–6 injections of 150–200 c.cm.—in some cases all plasma, in others at least half plasma—given intravenously. Treatment was ambulatory and the patients received a total of 800–1000 c.cm. Sometimes they developed fever, but as a rule there was no reaction of this kind. After every injection the patient was given Pyramidon, 0·3 g., which I think prevents the milder reactions. The intervals between injections depended on how the patient felt, but I usually gave one every second day.



(*a*) (*b*)

Patient aged 29 years with amenorrhœa for 10 months. (*a*) Endometrium before treatment, completely atrophic. (*b*) Endometrium 14 days after treatment, showing normal appearance.

Curettage before treatment produced more or less atrophic endometrium. After 3 injections of placental blood of 150 c.cm. each, and 3 injections of plasma in similar dosage, 5 patients showed a complete change in the endometrial structure from atrophy to the proliferative or secretory state. All 5 menstruated shortly after treatment, though they had been amenorrhœic for periods ranging from 5 months to 2 years. Another patient menstruated 20 days after the beginning of treatment but the mucosa remained atrophic. The remaining 5 patients did not react at all; one had not menstruated for 15 years and examination of the uterine mucosa showed tuberculous endometritis. I had removed the one remaining ovary of another woman a year before. She had developed menopausal symptoms which were not affected by placental blood, and no change was seen in the uterine mucosa. This case suggests that the action of placental blood does not depend on its folliculin content but on gonadotropic substances present in it. The remaining 3 unresponsive cases had not menstruated for periods ranging from 2 to 5 years, and were suffering from climacterium præcox. In all cases which menstruated or showed changes in the endometrium the size of the uterine cavity increased from 1 to 2·5 cm.

SUMMARY

A series of 34 patients who had had amenorrhœa for periods ranging from 4 months to 15 years received placental blood or plasma intravenously; 18 of them menstruated within 5–35 days of the end of treatment.

Of 11 patients showing atrophy of the endometrium before treatment, 6 had a normal endometrium after 5-6 intravenous injections of 150–200 c.cm. of placental blood or plasma.

These results indicate that placental blood is rich in gonadotropic substances.

". . . If colds and their coughs hadn't made a habit of coming and going in precisely the same way regardless of what we did for them, man would long since have coughed himself off the face of the earth."—THEODORE G. KLUMPP, *Science*, Aug. 1, 1941, p. 99.

# MENINGOCOCCAL INFECTION

R. C. DICKSON, M.D. TORONTO
D. MAGNER, B.SC., M.D. TORONTO
N. E. MCKINNON, M.B. TORONTO
N. B. MCGILLIVRAY, M.D. TORONTO, M.R.C.P.
MAJORS R.C.A.M.C. CAPTAINS R.C.A.M.C.
(*Divisions of Medicine and Pathology, No. 15 Canadian General Hospital, R.C.A.M.C.*)

SINCE the identification of the meningococcus by Weichselbaum in 1887, the clinical concept of meningococcal infection has been dominated by its most serious manifestation—meningitis. As early as 1899 Gwyn recovered meningococci from the blood of patients suffering from meningococcal meningitis, and in 1902 Salomon described meningococcal septicæmia without meningitis. Although of recent years reports (Applebaum 1937, Heinle 1939, Stott and Copeman 1940) of similar cases of meningococcal blood-stream infection have become more numerous, the disease is still regarded by most physicians as a clinical rarity.

A series of 26 patients suffering from meningococcal infection were admitted to No. 15 Canadian General Hospital in the period July, 1940, to June, 1941, inclusive. Of these 11 did not have meningitis on admission (though one, case 10, subsequently developed it) but had meningococcal septicæmia. We thus had an opportunity to observe the course of infection in these patients, and to compare their histories with those of meningitic cases seen in the same body of troops at the same time. The cases were sporadic, occurring in every month of the year. They came from Canadian troops stationed in England, but were not otherwise related to each other or to other recognised cases of meningococcal infection. For presentation the series is divided into two groups: an ameningitic and a meningitic.

### THE AMENINGITIC GROUP

The 11 patients without meningitis came to hospital under a variety of diagnoses, including influenza, arthritis, erythema nodosum and rheumatism. The diagnosis in 10 of the 11 cases was proven by growing *Neisseria meningitidis* from the patient's blood (table I). The clinical manifestations, however, were such as to render a diagnosis possible in most cases.

The onset was sufficiently definite to enable the patient to fix its date with fair precision. Thereafter the course was marked by striking remissions, varying greatly in length, and by even more striking relapses. The early symptoms of fatigue, malaise, feverishness, chilliness, occasional true rigor, aching pains in the limbs and back, and sometimes moderate intermittent headache, were those which characterise the onset of many acute infections. Other symptoms and signs of more particular diagnostic value were superimposed on this general picture of infection. These were localised muscle pain, localised joint pain and skin lesions.

The localised muscle pain, present in 10 of the 11 patients, differed sharply from the aching pain common in acute infection. Its onset was abrupt, associated with fever and general symptoms of infection, and often with localised joint pains and with crops of the skin lesions described below. While in some it was little more than stiffness, it was of sufficient severity to form the chief complaint of 5 of the patients. It was increased by movement. Its site could be localised accurately by the patient and was tender. The calf muscles were most commonly affected, less often those of the back, thighs and arms.

Localised joint pain, aggravated by movement, occurred in 8 of the patients and was a chief complaint in 3. Its onset, too, was abrupt and associated with symptoms of infection and frequently with a crop of skin lesions. In 3 cases the pain was associated with redness, swelling and increased heat; in 1 of these there was increased joint fluid. These 3 patients came to hospital with a diagnosis of arthritis. In some patients the joint pain seemed to be related to a tender skin lesion overlying the joint, while in others it was not associated with any demonstrable abnormality. The pain usually disappeared in a few days, only to recur in the same or in other joints. One or more joints were involved at one time, more commonly the large joints, but sometimes the small joints of the hands and feet.

Skin lesions appeared at some time during their illness in all the patients except one, case 8, whose illness was only of two days' duration before treatment. The spots appeared suddenly, in crops of a few or dozens, at any place on the body surface, but most commonly on the limbs and trunk. Their occurrence coincided with or closely followed the onset or recurrence of fever and general symptoms of infection. The patient's attention was drawn to them, not only by their appearance, but also because many were painful and tender. The spots varied in colour, size, palpability and tenderness. Most of them were clearly demarcated bright pink circular areas, 5–35 mm. in diameter, the smaller sizes predominating. They were regular in outline; some had a central dark purplish red spot or streak, and a few of the larger spots were darker and resembled somewhat the lesions of erythema nodosum. On pressure the pink zones faded, but the purplish red centres persisted, indicating hæmorrhage. Most of the larger lesions, and all those with hæmorrhagic centres, were palpable. Some were elevated slightly above the skin surface, others were deeper. Many of the lesions, particularly the larger ones, were moderately painful and tender. Often such spots marked the site of localised muscle or joint pain. Subsequent examination revealed changes in the lesions. After a few hours, or next day, some which had appeared at first as red macules had developed hæmorrhagic centres and become palpable. In two to four days the redness faded and the tenderness disappeared. Slight staining from the central hæmorrhage, and sometimes a small lump, persisted for a week or more. The lesions were in no way similar to the blotchy purpuric eruption commonly observed in cases of cerebrospinal fever and occurring in some of the meningitic cases in this series (table II).

The appearance of a crop, or crops, of the skin lesions, associated with fever, general symptoms of infection and localised muscle and joint pain, usually accompanied by leucocytosis, provided a clinical picture which strongly suggested meningococcal septicæmia.

Enlargement of the spleen was not observed in any of the cases. The only evidence of endocarditis found was that of a pre-existing aortic insufficiency due to rheumatic fever in childhood in case 8. No change in the character of the murmur was observed during his stay in hospital, and the course of the disease in this patient did not differ from the others. Under treatment he made a complete recovery from the meningococcal infection.

The cerebrospinal fluid was examined in 6 of the 11 cases, although none presented any clinical evidence of meningitis. In all the fluid was normal in cell and protein content and was sterile on culture.

In this group, 9 patients were treated with sulphapyridine during the ameningitic phase; 8 made a complete recovery after the administration of 34 g. of the drug in seven days, 12 g. being given in the first twenty-four hours. In case 3 the diagnosis was not made, and consequently treatment was not instituted until the disease had been present for three months. Although the infection was then cured by chemotherapy and did not recur, this soldier was left with residual joint pain, which necessitated lowering his medical category. Case 1 was not given chemotherapy and case 10 was not given sulphapyridine until meningitis developed. The case-histories of these 2 patients well illustrate features presented by most of the patients in the group. They also show certain features of special interest, and serve to stress the importance of recognition and treatment of meningococcal septicæmia.

CASE 1.—A gunner, aged 39. He had been well until May 23, when he had developed malaise, chilliness, feverishness and aching pain in the back and limbs. He was evacuated to a military hospital. Temperature was 103° F.; leucocyte count 17,000 with 77% neutrophils. Meningitis was suspected, but the C.S.F. was normal and sterile on culture. On May 25 he developed pain in the knees, ankles and shoulders. He was transferred to an E.M.S. hospital and treated for rheumatism during the next five weeks. During this time he noted repeated crops of spots in the skin many of them tender, appearing in association with recrudescence of fever, muscle pain and joint pain. On July 6 he was admitted to this hospital. At that time the right knee and ankle were

painful and swollen; movement was restricted by pain. Many red, palpable, tender spots about the size of a sixpence were scattered over the limbs and trunk. Some of these had hæmorrhagic centres. From July 6 to 28 he had repeated remissions and relapses. Thereafter he remained free of symptoms and was sent to a convalescent depot on Aug. 12. A diagnosis of arthritis was recorded.

In retrospect it appears certain that this patient suffered from meningococcal septicæmia, and that the diagnosis was missed both by ourselves and at the two other hospitals. The two blood samples taken while in this hospital did not show any growth, but such evidence is quite inadequate (see table I) to exclude the diagnosis

TABLE I—THE AMENINGITIC GROUP

| Case | Admitted | Duration (days) | Muscle pain | Joint pain | Skin lesions | Leucocyte count | No. of blood samples | Positive |
|---|---|---|---|---|---|---|---|---|
| 1 | July 6, 1940 | 45 | + | + | + | 17,000 | 2 | 0 |
| 3 | July 31 | 90 | + | + | + | 18,000 | 2 | 1 |
| 6 | Aug. 30 | 17 | + | − | + | 18,000 | 1 | 1 |
| 8 | Oct. 25 | 2 | − | − | − | 23,000 | 1 | 1 |
| 10 | Nov. 23 | 12 | + | + | + | 11,000 | 2 | 1 |
| 12 | Jan. 1, 1941 | 60 | + | + | + | 9000 | 4 | 2 |
| 15 | Feb. 18 | 15 | + | + | + | 14,000 | 10 | 4 |
| 17 | Feb. 25 | 27 | + | + | + | 10,000 | 4 | 1 |
| 20 | March 15 | 7 | + | + | + | 22,000 | 6 | 4 |
| 21 | March 24 | 28 | + | + | + | 17,000 | 21 | 2 |
| 26 | June 14 | 33 | + | + | + | 10,000 | 14 | 12 |

of meningococcal septicæmia in a patient presenting the above clinical findings. This patient was still free from recurrence about three months later, having made, apparently, a spontaneous recovery, but he was invalided home to Canada on account of residual joint pain.

CASE 10.—A sapper, aged 19. He had been in good health until Nov. 16, 1940, when he became suddenly ill with fatigue, malaise, feverishness, chilliness, headache and localised pain in the right calf. He felt better for the next two days, during which he remained on duty. On Nov. 19 he became more ill; temperature 104° F.; a crop of red tender spots appeared in the skin; he was evacuated to a dressing station where he again had a short remission. On the 21st he had recurrence of fever and more spots; and on the 23rd, when there was fever again and more spots, he was transferred to this hospital. Temperature 103° F.; many skin lesions present, some tender and many palpable with hæmorrhagic centres. Leucocyte count 11,000 with 88% neutrophils. Next day his temperature was normal and the spots fading. On the 25th he had a rigor; temperature rose to 104·6° F. He complained of malaise, moderate headache and general aching pain with more severe and localised pain in the left elbow. There were many new skin lesions, one of which, very tender, was situated over the left elbow. Lumbar puncture revealed clear fluid under normal pressure; 3 lymphocytes per c.mm.; Pandy test negative; fluid sterile. A blood sample taken on this day yielded *N. meningitidis* group I on Nov. 28. By this time, however, the patient was afebrile and symptom-free. No specific treatment was instituted. He felt well and was up and about the ward until Dec. 16 (18 days intermission). On that day he again had a rigor and his temperature rose to 103° F. He complained of malaise and aching pains in limbs and back. A new crop of spots appeared. He developed headache, which rapidly became severe, slight neck pain and stiffness. Blood taken at this time was sterile. C.S.F.: 100 neutrophils per c.mm.; protein 40 mg. per 100 c.cm.; no organisms seen on direct smear, but culture yielded *N. meningitidis* group I. Under treatment with sulphapyridine the patient made a complete recovery, although the C.S.F. cell-count rose to 1200 during the first 12 hours of treatment.

This case was thus observed first in the ameningitic phase of the disease. Then, after a period of freedom from symptoms, the infection again became manifest, but this time meningitis developed. The case serves to stress the close association between the ameningitic type of meningococcal infection and the meningitic type, a relationship that is further demonstrated on consideration of the meningitic group.

### THE MENINGITIC GROUP

The clinical histories of the patients comprising this group indicated the presence of infection for periods varying from a few hours to several weeks before the onset of meningitis. While it is impossible to identify precisely the beginning of meningeal inflammation, there are grounds for assuming that it approximates in time to the onset of severe persistent headache. Although such headache was the chief complaint of all the patients who were conscious at the time of admission, in no case was it the first symptom of the illness. That headache of this type may accompany very early meningeal involvement is apparent from case 10, where lumbar puncture was done within four hours of the onset of persistent headache, the Pandy test was negative, the C.S.F. cell-count was only 100 neutrophils, and culture yielded *N. meningitidis* group I. The premeningitic period shown in table II refers therefore to the time between the onset of symptoms and signs of infection, and the onset of severe persistent headache. This premeningitic period lasted from one to seven weeks in 5 cases, from one to six days in 4 cases, and from three to sixteen hours in 6 cases. In one case the information was not recorded. The early symptoms were, as in the ameningitic group, those commonly characteristic of the onset of acute infection. However, in an appreciable number of the patients there were additional features which indicated a more specific diagnosis.

In 8 of the 9 cases in which the premeningitic period lasted longer than one day, the signs and symptoms occurring in this phase of the disease were clearly defined. These 8 patients gave a history of localised joint pain, associated with localised muscle pain in 6, and with skin lesions of the type described above in 5. Further, all 5 patients in whom this period exceeded a week gave a history of remissions and relapses. In short, the illness

TABLE II—THE MENINGITIC GROUP

| Case | Admitted | Duration of ameningitic phase | Muscle pain | Joint pain | Skin lesions | Purpura | Leucocyte count | Blood culture | C.S.F. | | | Duration of meningitis before treatment (hr.) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | Cells | Film | Culture | |
| 2 | 1940 July 17 | ? | ? | ? | − | − | .. | .. | 1200 | − | .. | 12 |
| 4 | Sept. 11 | 3 hr. | ? | ? | − | − | 31,000 | + | 3600 | + | + | 12 |
| 5 | Sept. 29 | 16 hr. | − | + | − | + | 23,000 | + | 40,000 | + | + | 36 |
| 7 | Oct. 24 | 15 days | + | + | − | − | 14,000 | − | 2500 | − | + | 10 |
| 9 | Nov. 7 | 4 days | − | − | − | − | 17,000 | − | 20,000 | + | + | 24 |
| 10 | Nov. 23 | 30 days | + | + | + | − | 12,000 | − | 100 | − | + | 5 |
| 11 | Dec. 10 | 6 days | ? | + | − | − | 18,000 | − | 12,000 | − | + | 24 |
| 13 | 1941 Jan. 2 | 30 hr. | − | + | − | − | 19,000 | − | 6500 | + | + | 36 |
| 14 | Jan. 13 | 6 hr. | − | − | − | + | 17,000 | − | 16,000 | − | − | 17 |
| 16 | Feb. 21 | 12 hr. | − | − | + | + | 26,000 | − | 37,000 | + | + | 12 |
| 18 | Feb. 27 | 3 hr. | − | − | + | − | 24,000 | + | 9000 | + | + | 48 |
| 19 | Mar. 11 | 11 days | + | + | + | − | 14,000 | − | 6500 | − | − | 48 |
| 22 | April 2 | 12 hr. | − | + | − | + | 20,000 | + | 250 | − | + | 8 |
| 23 | April 8 | 2 days | + | + | + | − | 22,000 | − | 9000 | + | + | 12 |
| 24 | April 30 | 14 days | + | + | + | − | 16,000 | − | 9000 | + | + | 10 |
| 25 | May 7 | 49 days | + | + | + | − | 10,000 | − | 1200 | − | + | 24 |

of these patients before the onset of meningitis was essentially similar to those of the patients in the ameningitic group. In 3 of the 6 cases in which the premeningitic period was less than one day the symptoms were essentially similar to those of the ameningitic group—muscle pain, joint or skin lesions either singly or in combination. In 2 cases the information was not

obtained. In case 14 it is known that such signs or symptoms were not present although the patient was ill with general symptoms of infection for six hours before the appearance of any headache. The clinical records of some of the patients are even more enlightening than the tabulated data. For example, in case 5 the soldier first reported to his regimental medical officer because of pain in the right ankle and knee, and was evacuated to a casualty clearing station with a diagnosis of rheumatism. In case 22 the patient complained of sudden severe pain in the right shoulder, approximating in time to the onset of the headache. It should be pointed out here that the patients suffering from meningitis seldom gave this history at the time of admission to hospital. The more distressing symptoms of meningitis tended to obliterate the memory of the milder symptoms of the earlier illness. However, with the disappearance, under treatment, of the headache, irritability and mental confusion the patients recalled their preceding illness vividly.

It is apparent from table II that the cases varied greatly in severity from mild to fulminating. Meningococci were recovered from the cerebrospinal fluid in 13 of the 16 cases. In 1 the fluid was not cultured, in 2 it failed to yield any growth. These 3 were clinically typical cases of cerebrospinal fever. The intervals between the onset of meningitis and the beginning of treatment were from five to seventy-two hours.

In addition to the usual symptomatic treatment, sulphapyridine was used as in the ameningitic cases, but was continued for ten days and a total of 40 g. was given. In all but the mildest cases the dosage by mouth was augmented by the intravenous administration of 2–4 g. of sodium sulphapyridine at the onset of treatment. Unconsciousness or persistent severe vomiting made necessary the continuation of the intravenous therapy in cases 5, 14 and 22. Blood levels of 4·2–12 mg. of free sulphapyridine per 100 c.cm. and C.S.F. levels of 2·7–10 mg. per 100 c.cm. were obtained during the first forty-eight hours.

Of the 16 patients, 12 made a rapid and complete recovery, all symptoms disappearing in three to five days. In these the C.S.F. pressure, cell-count and protein content fell rapidly, but in some several weeks passed before the cell-count and protein were entirely normal. Deafness, present in 3 patients on admission, cleared entirely in 2; the third was left with slight nerve deafness not sufficient to lower his medical category. This patient had mild intermittent headache which persisted for ten weeks. One patient continued to complain of slight headache and neck pain for eight weeks; in this case, although the cell-count and protein content returned rapidly to normal, the C.S.F. pressure continued high; the end-result is not yet known. Cases 5 and 22 died.

Case 5, a fulminating infection with severe meningitis, was comatose on admission and the cell-count in the spinal fluid was 40,000; *N. meningitidis* was recovered from both blood and C.S.F. The patient showed some improvement and subsequent samples of blood and C.S.F. failed to yield growth. In spite of this temporary improvement, the coma deepened, breathing became rapid, stertorous and irregular, pulse and temperature rose. Clinically death occurred from respiratory failure. At necropsy there was much œdema of brain and spinal cord with flattening of the cerebral convolutions, and the brain was compressed downwards with herniation of the hippocampal unci through the tentorial notch, and of the cerebellar tonsils through the foramen magnum. This cerebellar pressure cone was well developed. The pial blood-vessels were intensely injected, but practically no meningeal exudate was present. Death was apparently due to medullary compression consequent on increased intracranial pressure.

Case 22 was desperately ill on admission, with extensive purpura and showed only 250 cells in the C.S.F.; this, however, yielded meningococci, as did the blood. With treatment there was temporary clinical improvement and both blood and C.S.F. became sterile. The early improvement was followed by acute left heart-failure, manifested by acute pulmonary œdema and rising pulse-rate. He died thirty-six hours after admission. At necropsy, although the pial vessels were extremely injected and the brain somewhat œdematous, there was a complete absence of gross meningeal exudate, and microscopically several sections had to be studied before evidence of scanty cellular exudate was seen. Generalised purpuric hæmorrhages and an extremely flabby heart, the chambers of which were much dilated, were indications of the severe toxæmia.

### BACTERIOLOGY

Blood samples were planted in glucose broth. C.S.F. was drawn directly at the bedside into small vials containing sloped Löffler's medium. It is evident (tables I and II) that recovery of the organism from the blood in non-fulminating cases was largely a matter of chance. For example, twenty-one samples of blood from case 21 yielded only two positive cultures. Growth was demonstrable in some cultures in twenty-four hours, but in others longer periods of incubation up to ten days were required. This variation was found in cultures obtained at different times from the same patient. For instance, one blood sample from case 26 yielded growth in twenty-four hours; another required seven days before growth was demonstrable by film or sub-culture.

All the strains isolated gave typical fermentation of glucose and of maltose. They were tested for agglutination with specific antisera by the late Dr. W. M. Scott and Dr. Marion Watson, from whose reports the following summary is made:

Of the 10 strains isolated from the ameningitic group cases 6 and 26 were group I; cases 12 and 20 were group I, type III; case 10 was group I, uncommon type; case 15 was group I, aberrant type; case 17 was probably group II; case 8 was agglutinated by group I and group II antisera; cases 3 and 31 were not agglutinated by either. So far as the agglutinative type was concerned, therefore, the strains exhibited considerable variety. Of 10 of the strains isolated from the meningitis cases, 5 (cases 16, 22, 23, 24 and 25) were group I, type III; 3 (cases 9, 11 and 18) were group II; 1 (case 10) was group I, uncommon type; 1 (case 13) group I, aberrant type. Strains isolated from cases 5 and 7 were not sent to Dr. Scott, but tests in the laboratory of this hospital showed them to be group I. One strain, case 4, was not tested. It is to be noted that meningitic cases from whom the same agglutinative type was isolated showed widely different premeningitic periods. For instance, cases 16 and 22, from whom group I, type III, strains were obtained, each had a premeningitic period of twelve hours, while cases 24 and 25, from whom the similar group I, type III, strains were obtained, had premeningitic periods of two weeks and seven weeks respectively.

### DISCUSSION

The fact that the number of cases of ameningitic meningococcal septicæmia approached the number of meningitic cases in this series strongly supports Heinle's statement that "meningococcic septicæmia can no longer be regarded as a rare disease." The character of the skin lesions, with their sudden occurrence in crops, associated with symptoms of infection, fever and leucocytosis in the presence of proven bacteræmia, provides good evidence that they are due to localisation of organisms in the skin. The isolation by Kennedy (1926) of gram-negative diplococci from what appears to have been a similar lesion is strong confirmation of this view. So, too, the muscle and joint pain, abrupt in onset and often occurring at the same time as the skin lesions in the proven bacteræmic cases, seems to be due to similar localisation of bacteria in deeper tissues. The recovery by Still (1898) of a gram-negative diplococcus from a tendon sheath—the site, apparently, of a similar lesion—is corroborative evidence.

The occurrence of skin lesions, localised muscle pain or localised joint pain during the premeningitic phase of meningitic cases is strong, if not conclusive, evidence that the premeningitic illness was really due to meningococcal septicæmia. More of the ameningitic cases might have developed meningitis, like case 10, had the infection not been interrupted before that incident. The course of the infection as exhibited by the patients in this series as a whole appears to have been the development of bacteræmia followed by localisation of bacteria in the skin, skeletal tissues and sometimes the central nervous system. If the nervous system was not involved early, remissions and relapses occurred and chronic meningococcal septicæmia developed.

In some of the meningitic cases with longer premeningitic periods the diagnosis might well have been made and

effectual treatment given before the onset of meningitis. This would have resulted in an increase in the number of ameningitic cases in the series, and—what would have had more significance—a corresponding reduction in the number of cases of meningitis treated in this hospital. In others with a shorter premeningitic phase appreciation of the significance of such signs and symptoms might have suggested the character of the infection and have led to closer supervision and earlier treatment. It is still important that cases of meningococcal meningitis should be treated at the earliest possible moment; further reduction in mortality seems to depend on such early treatment.

There is no reason to suppose that a peculiar susceptibility or resistance of the host was operative in this series. Some of the patients had recently arrived in this country, others had been here for a year or more. There is nothing to suggest that the troops from which they came differed in any way from their fellows, or that the environment in which they lived affected their reaction to the infection. The fact that organisms of several different agglutinative types were recovered from both the ameningitic and meningitic groups goes far to exclude the possibility that a special characteristic of the organism was important in determining the course of the infection. It appears unlikely, therefore, that the findings here reported are peculiar to this group.

SUMMARY

A series of 26 cases of meningococcal infection, occurring in Canadian soldiers stationed in England and admitted to a Canadian general hospital between July, 1940, and June, 1941, is reported.

Of these patients, 11 did not have meningitis on admission, but suffered from meningococcal septicæmia; only one of these subsequently developed meningitis. The clinical findings in this group include the presence of characteristic skin lesions and of localised muscle pain and joint pain.

Most of the 16 meningitic patients had a premeningitic phase in which the signs and symptoms were identical with those of the patients in the ameningitic group, and were no doubt also due to meningococcal septicæmia.

REFERENCES

Applebaum, E. (1937) *Amer. J. med. Sci.* **193**, 96.
Gwyn, N. B. (1899) *Johns Hopk. Hosp. Bull.* **10**, 112.
Heinle, R. W. (1939) *Arch. intern. Med.* **63**, 575.
Kennedy, J. C. (1926) *J. R. Army med. Cps*, **47**, 6.
Salomon, H. (1902) *Berl. klin. Wschr.* **39**, 1045, quoted by Heinle.
Still, G. F. (1898) *J. Path. Bact.* **5**, 147.
Stott, A. W. and Copeman, W. S. C. (1940) *Lancet*, **1**, 1116.

# PARADOXICAL CEREBRAL EMBOLISM

## WITH RECOVERY

ALAN GRAHAM PORTER, M.B. CAMB.
HOUSE-PHYSICIAN AT THE EMERGENCY HOSPITAL, CAMBRIDGE

PARADOXICAL embolism, by definition, is the passage of an embolus, usually originating in a thrombus of a systemic vein, direct from the right to the left side of the heart, without traversing the pulmonary vessels, to produce a systemic arterial embolism. The condition was first described by Cohnheim (1876), and Zahn (1881) demonstrated an embolus in situ astride a patent foramen ovale. Von Recklinghausen (cited by Thompson and Evans 1929–30) suggested the term "paradoxical," rather than "crossed" embolus which had previously been used. From an analysis of 13,234 consecutive autopsies, Thompson and Evans found that paradoxical embolism was responsible for death in 4% of all cases of cerebral embolism, and mentioned that diagnosis during life can never be quite certain. The following is a case of paradoxical cerebral embolism in which the patient recovered.

A gunner, aged 26, admitted to hospital on March 7, 1941, complaining of pain and swelling behind left knee of 24 hours' duration. Had had varicose veins for some years but they had never given trouble. Tender and swollen varicose vein behind left knee; diagnosis of phlebitis made and treatment instituted. On March 11 thrombosis had spread up great saphenous vein for several inches. On evening of the 21st patient was lying on his bed, having been allowed up for a day or two, and when spoken to was found to be unconscious. Soon regained consciousness, but speech slurred, both pupils widely dilated and generalised tremor of limbs. Next morning complete flaccid left-sided hemiplegia, fine nystagmus to left, paralysis of left external rectus oculi, left palate and left lower face. Incontinence urine, which lasted 24 hours. On 23rd paralysis had become spastic, with increased deep reflexes and absent abdominal reflexes on left and left extensor-plantar response. No alteration of sensation or any other abnormal sign in central nervous system. Lumbar puncture produced normal fluid under normal tension. No enlargement of heart or cardiac murmurs; blood-pressure 125/85. Chest showed no evidence of pulmonary embolism. Temperature and respirations normal. X ray of chest at later date normal. Urine normal.

By March 27 movement returning to left foot and knee, and by end of April patient was moving about ward with help. On May 24 examination prior to a medical board revealed: slight left-sided lower facial weakness, weakness of convergence of left eye with bilateral nystagmus on looking to left; some weakness of left hand and arm and very slight weakness of left leg and foot; left abdominal reflexes diminished, with accentuation of deep reflexes on left and left extensor-plantar response. All these signs were less a month later and patient was then walking about freely.

### DISCUSSION

The embolism had presumably occurred in the right middle cerebral artery, in the region of the internal capsule—the commonest site for such a lesion though Hartfall (1931) recorded a case of paradoxical embolism in the basilar artery.

There are two routes by which an embolus could pass directly to the left from the right side of the heart: through a patent foramen ovale or through an opening in the interventricular septum. Pressure is higher in the left than in the right auricle, and the foramen ovale is usually guarded, on the left side of the interauricular septum, by a flap-valve. The head of pressure on the left side is sufficient to keep the flap closed and so to ensure the competence of the valve. From the mechanical point of view an alteration of pressure between the two sides of the heart is required to destroy the competence of the valvular foramen ovale; thus a rise in the right auricular pressure and a fall in that of the left auricle would cause the valve to open. Haggart and Walker (1923) found that a partial occlusion of the pulmonary artery in cats caused a rise of pressure in the right side of the heart, accompanied by a fall of pressure in the left side. This mechanism has been supposed to operate when an embolus lodges in the pulmonary artery, and Thompson and Evans have advanced three criteria for the production of paradoxical embolism:

1. At least a third of the diameter of the pulmonary artery must be occluded by an embolus: less than this is not sufficient to alter the pressures materially, while occlusion of more than a half results in immediate death.
2. A second embolus must shortly follow the first and appear in the right auricle.
3. The second embolus must be small enough to pass through the foramen ovale, now rendered patent through alteration in intracardiac pressure.

In the case here described there was no clinical evidence of a pulmonary embolus; physical examination of the lungs was normal, respiration-rate unaltered, temperature normal, there was no cough and no sputum, and a radiogram of the chest, when the patient was well enough to have one taken, was normal. Of Thompson and Evans's 5 cases of paradoxical embolism, only 2 showed evidence of pulmonary embolus, and it seems that though this occurrence is possibly a mechanical necessity in the cases of valvular foramen ovale, it is not essential to paradoxical embolism. Two other possibilities exist. First, a widely patent foramen ovale could allow the passage of an embolus without previous pressure changes. In 1100 consecutive autopsy records examined by Thompson and Evans at the London Hospital, patency of the foramen ovale was found in 35% (29% up to 2 cm. and 6% up to 7 cm.). In a further 24 cases dying from pulmonary embolism, and found at autopsy to have a patent foramen ovale, there was no evidence of paradoxical embolism. Sir Thomas Lewis (1934) stated that

patency (which he distinguished from mere persistence by the size of the aperture) of the foramen ovale was very rare; neither condition, he said, gave rise to signs. It seems possible that a widely open foramen, giving rise to no physical signs, could transmit an embolus in the absence of pressure changes.

A second theory, put forward as a possible alternative, is that the embolus arrives in the right auricle, coils up over the tricuspid valve and blocks it sufficiently to cause the momentary rise in pressure necessary to force open the valve guarding the patent foramen ovale. The embolus is then swirled through the foramen to the left heart and so to the systemic circulation; the tricuspid valve acts normally again, the foramen ovale flap-valve closes and the pressures are restored to normal. I do not suggest that these alternatives are mutually exclusive, but that either may be in operation, according to the state and size of the foramen ovale.

Diagnosis can never be certain, but Thompson and Evans stated that "If a patient, the subject of venous thrombosis, develops cerebral embolism . . . and if in such a patient there is no clinical evidence of any cardiovascular disease present, then it may be justifiable to assume that the embolus is of the paradoxical variety." In my case there were no clinical or radiological signs of cardiovascular abnormality. The circulation-rate was estimated with the object of demonstrating, if possible, the existence of a patent foramen ovale. The arm-to-tongue method was employed, using Suprachol. The time was 12 sec., the normal for young men being 12–16 sec. Although the result was inconclusive it was at least at the rapid extreme of normal range.

The differential diagnosis lay between paradoxical embolism and thrombophlebitis migrans. Ryle (1936) says that thrombophlebitis migrans is never due to varicosity, that it is essentially migratory, affecting multiple small lengths of superficial veins, and is accompanied by fever; hæmoptysis, pleurisy and hæmaturia may also occur. Paradoxical embolus, therefore, was confidently diagnosed in this case. Recovery was virtually complete. I can find no record of a previous case of paradoxical cerebral embolism which recovered, with the exception of case 1 in Thompson and Evans's series, which they described as unique.


### SUMMARY

A case of paradoxical cerebral embolism is described, in a young man who recovered completely.

There was no evidence of previous pulmonary embolus.

The embolus may have reached the systemic circulation either by passing directly through a widely patent foramen ovale; or (if the patent foramen was of the valvular type) by causing temporary obstruction to the tricuspid valve so that the pressure in the right auricle rose above that in the left auricle, and the embolus was swept through the foramen.


I wish to thank Dr. L. C. Martin, who had charge of the case, and Dr. Leslie Cole, who estimated the circulation-rate.

### REFERENCES


Cohnheim, J. (1887) *Allgem. Path.* Berlin, **1**, 134.
Haggart, G. E. and Walker, A. M. (1923) *Arch. Surg.*, Chicago, **6**, 764.
Hartfall, S. (1931) *Lancet*, **1**, 700.
Lewis, T. (1934) Diseases of the Heart, London, p. 264.
Ryle, J. A. (1936) Natural History of Disease, London, p. 331.
Thompson, T. and Evans, W. (1929–30) *Quart. J. Med.* **23**, 135.
Zahn, F. W. (1881) *Rev. méd. Suisse rom.* **1**, 227.


For the treatment of scabies MESSRS. BOOTS have issued a solution of benzyl benzoate called Scobenzol. This contains benzyl benzoate 25%, soft soap 25%, and isopropyl alcohol 50%.

BRITISH DRUG HOUSES have prepared a thick cream containing titanium dioxide, zinc oxide and small quantities of purified silicates in a non-fatty base for application in exudative dermatitis and similar conditions. "Siccolam" is said to have dehydrating properties similar to calamine lotions but of much greater degree, and it can be used either alone or with the addition of sulphur, tar, or other medicaments. It is issued in 2 oz. and 4 oz. collapsible tubes.

# ISOAGGLUTININ CHANGES
## AFTER TRANSFUSION OF INCOMPATIBLE BLOOD AND SERUM


P. L. MOLLISON, M.B. CAMB., M.R.C.P. — I. MAUREEN YOUNG, B.SC.

*(South-west London Blood-supply Depot)*


LITTLE attention has so far been paid to serological changes in the recipient after the transfusion of incompatible blood. There are only 3 recorded cases in which such changes have been noted.

Rø (1937) reports the case of a patient of group O who received 500 c.cm. of group A blood. Although preliminary cross-matching showed no agglutination of the donor's cells by the recipient's serum, when the test was repeated with serum obtained two days after the transfusion agglutination occurred up to a dilution of 1/20. At the end of five weeks the agglutinating power of the recipient's serum for A cells had increased further and agglutination occurred in a dilution of 1/200. Four weeks later the titre had fallen to 70 (the titre being expressed as the reciprocal of the greatest dilution in which agglutination is noted). Rø suggests that the recipient's serum contained only a hæmolysin for A cells before the transfusion and that the introduction of A cells stimulated the production of an agglutinin. In any case, it seems clear that the agglutinin titre rose rapidly during the period following the transfusion.

Wiener (1941) has published details of 2 cases, both of which had been referred to previously (Wiener 1939). The first patient, of group O, received 500 c.cm. of group B blood. Six hours after the transfusion, which was followed by a rigor and hæmoglobinuria but no serious sequelæ, it was observed that whereas the titre of the anti-A isoagglutinin was 32, that of the anti-B agglutinin was as low as 1. Further estimations were made at short intervals, and it was found that while the titre of the anti-A isoagglutinin remained constant, that of the anti-B agglutinin rose steadily, reaching a peak, at the thirteenth day, of 512. The same figure was found when the serum was re-titrated on the twenty-fourth day after the transfusion. The other case was less closely observed. Six days after the transfusion of incompatible blood (of group AB, the patient belonging to group A), it was found that the titre of the anti-B agglutinin was 128; and eight days later 256. It is concluded that these changes represent an absorption of isoagglutinin by the injected agglutinogen, followed by an immune response to the foreign agglutinogen.

In only one of these 3 cases were frequent titrations of the recipient's serum carried out, and in that observations were only extended up to the twenty-fourth day after transfusion. It may therefore be of interest to record the following case in which, after the transfusion of incompatible blood, the isoagglutinins in the serum of the recipient were repeatedly titrated and the changes were followed for some months. The results obtained are in substantial agreement with those of Rø and Wiener, but changes in the "other agglutinin" were also found,—i.e., after the transfusion of group B blood to a person of group O not only was the titre of the anti-B agglutinin affected but also that of the anti-A agglutinin. These changes were traced to the use of a serum of group different from that of the patient.

### CASE-RECORD

A married woman, aged 32, was admitted to hospital at 1 A.M. on Sept. 16, 1940, half an hour after receiving injuries caused by a high-explosive bomb. The injuries were mainly due to falling masonry and included fractures of both legs. She was found to be "shocked" and was treated with warmth, morphia and the transfusion of blood and plasma. After receiving 540 c.cm. of citrated stored blood 3 days old (equal to 360 c.cm. whole blood) and 250 c.cm. of pooled plasma, she improved sufficiently for the doctors in charge to leave her for the night. Next morning it came to our notice that the bottle of blood that had been given was not of group O, as had been assumed, but of group B. The patient was visited by us for the first time at 10 A.M., some eight hours after the transfusion had been given. She was then in a very poor condition. Her lips and nails were ashen grey and her skin very cold. No pulse was palpable at either wrist or over either brachial artery and no sounds could be heard at the latter site on auscultation. We were told that although no untoward

symptoms had occurred during the transfusion, no great improvement had followed; the patient's condition had deteriorated since, particularly during the last three hours.

After a preliminary intravenous injection of 150 c.cm. of 3% sodium-citrate, 1500 c.cm. of pooled citrated plasma, 100 c.cm. of four-times normal reconstituted serum and 2 pints of citrated blood (group O) were transfused. The clinical condition improved steadily throughout the transfusion and four hours from the beginning of this treatment, when all but the last 500 c.cm. of blood had been given, the blood-pressure was 116/80 mm. Hg and the extremities had become quite warm.

A quarter of an hour after the preliminary intravenous injection of alkali the patient was catheterised and 95 c.cm. of blood-stained urine was withdrawn. The urine was slightly acid to litmus and had probably all been formed many hours previously, since the blood-pressure was still unrecordable at this time. Very many red cells and some leucocytes but no casts were found in the centrifuged deposit of this specimen; the supernatant fluid only contained 0·7% hæmoglobin (Haldane). The patient was catheterised again at 12.45 P.M., when 170 c.cm. of urine was withdrawn; this was neutral to litmus. On centrifuging, it was apparent that the red colour was due almost entirely to red blood-cells, the supernatant fluid containing only a trace of hæmoglobin as measured by the benzidine test.

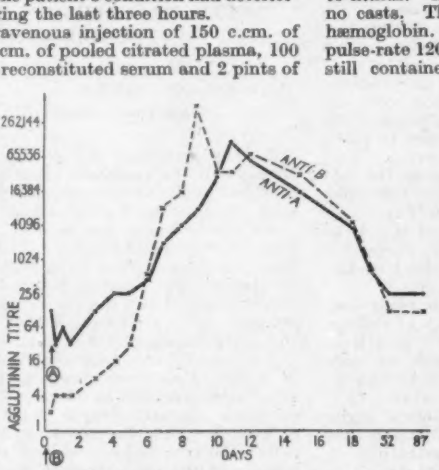



FIG. 1—Changes in titre of serum isoagglutinins after transfusion of (1) group B blood (at B), (2) concentrated serum of group A (at A). Recipient was group O.

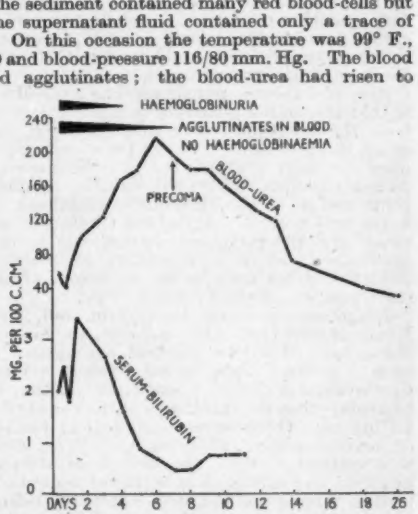



FIG. 2—Findings after incompatible transfusion.

A venous sample was first obtained eight hours after the initial transfusion and the findings were: hæmoglobin 66%, serum-bilirubin 2 mg. per 100 c.cm., serum-proteins 4·3%, blood-urea 55 mg. per 100 c.cm.; blood group O. Microscopical examination of a suspension showed fair-sized agglutinates which were not increased by the addition of anti-A or anti-B serum. A sample of serum was obtained at the same time and titrated with A and B cells from the donors normally used by this laboratory. The technique employed is that recommended by Taylor and Prior (1938); the end-point is read microscopically and clumps of 3–5 cells are taken as evidence of agglutination. The titre of the anti-A agglutinin was 128 and of the anti-B only 2 (see fig. 1). At 12.45 P.M., after the patient had received 1500 c.cm. citrated plasma and 100 c.cm. of four-times normal serum, a second venous sample was taken and examined. The hæmoglobin had fallen to 42% while the plasma-proteins had risen to 4·7%. The serum-bilirubin was 2·5 mg. per 100 c.cm., and the blood-urea 45 mg. per 100 c.cm. (see fig. 2). Microscopical examination showed rather bigger agglutinates than in the first smear. The titre of the anti-A agglutinin had fallen to 32, while that of the anti-B had risen slightly to 4.

After the further transfusion of two bottles of blood and 150 c.cm. of 3% citrate, another venous sample was obtained (5.20 P.M.). The hæmoglobin was now 49%, serum-bilirubin 1·8 mg. per 100 c.cm., serum-proteins 4·9% and blood-urea 75 mg. per 100 c.cm. The titre of the anti-A agglutinin was 64 and of the anti-B again 4.

From the time when the patient was first seen by us, an attempt was made to measure the fluid intake and the urinary output. During the first twenty-four hours 3000 c.cm. of lemon squash containing 35 g. of potassium citrate was given (as advised by Bushby and others 1940), and 2000 c.cm. of the same mixture was given during the subsequent twenty-four hours. A rather incomplete record of the fluid intake and urinary output was kept, but it was clear that there was a large negative water balance up to the eighth day, although the urinary output never fell to really low levels.

The patient was visited again on the morning of the 17th, some thirty hours after the incompatible transfusion. Her clinical condition was surprisingly good. She was lucid and not in pain. Her skin looked faintly yellow. She had been catheterised at 5 A.M., and 70 c.cm. of urine had been withdrawn. This specimen contained albumin and was neutral to litmus. The sediment contained many red blood-cells but no casts. The supernatant fluid contained only a trace of hæmoglobin. On this occasion the temperature was 99° F., pulse-rate 120 and blood-pressure 116/80 mm. Hg. The blood still contained agglutinates; the blood-urea had risen to 101 mg. per 100 c.cm., the serum-bilirubin to 3·2 mg. per 100 c.cm. and the serum-proteins to 5·1%. The titre of the anti-A isoagglutinin was 32; that of the anti-B agglutinin still 4.

On the 18th the patient was better, although the blood-pressure was 136/102 mm. Hg and the blood-urea 126 mg. per 100 c.cm. The serum-bilirubin had fallen a little (2·7 mg. per 100 c.cm.). A smear of the blood showed only a few small agglutinates. The titre of the anti-B isoagglutinin had risen to 8 and that of the anti-A isoagglutinin to 128. The urine was alkaline to litmus, and the sediment contained a few red blood-cells and pus and epithelial cells, but once more no casts. During the past twenty-four hours she had passed only 10–20 oz. of urine, compared with a fluid intake of 80 oz.

Until the 22nd (the 7th day) the patient appeared to improve steadily, despite a consistently raised diastolic pressure and a steadily mounting blood-urea. During this period agglutinates were found in the blood, but they became progressively smaller and actually were last seen on the 23rd. From the 18th onwards the titre of both anti-A and anti-B isoagglutinins rose steadily, and, as will be seen from fig. 1, reached very great heights during the period Sept. 24–27 (9th to 12th days). Between Sept. 23 and Oct. 11, when the titrations were read, it was noted that hæmolysis occurred in the first or first and second dilutions with both A and B cells.

On Sept. 23 the patient was much worse. She was very drowsy, her respirations were deep and there was a heavy brown fur on the tongue; she was considered to be in precoma. The blood-pressure was 150/100 mm. Hg. On this and the subsequent two days the patient was made to sweat profusely by giving Dover's powder and aspirin and heating her with electric blankets, &c. Whether as the result of the sweating or not, she was much better on the 24th, and the urinary output increased from this day onwards. On the 25th the improvement was maintained and the blood-pressure had fallen to 136/80 mm. Hg. From this time onwards, recovery was uneventful from the medical point of view.

During the ten days after the transfusion, two attempts were made to perform renal-function tests. Neither was wholly satisfactory, but both revealed an unequivocal degree of impairment of renal function. On Sept. 21 the clearance was 18% of normal and on the 26th, 30% (van Slyke). On the 26th the urine contained a trace of albumin and a few epithelial and granular casts. The urea-clearance test was repeated on Oct. 4 and was then 50% of normal.

Further examinations of the serum were made during the following months. A slow reduction in the titre of both isoagglutinins was found. From the abnormally high levels reached two weeks after the transfusion the titres gradually fell towards normal.

## DISCUSSION

The changes in the titre of the anti-B isoagglutinin will be seen to be of the same nature as those described by Wiener; they consist of an initial reduction, presumably due to an absorption by the transfused group B blood, followed by a big increase, presumably representing an immune response. The first specimen in our case was obtained eight hours after the transfusion, and thus may be compared with the first specimen in Wiener's case, obtained after 6 hours. The titre of the anti-B isoagglutinin was found, as in Wiener's case, to be extremely low. Thereafter there was a steady rise in titre, and the peak was reached on about the eighth day (not before the thirteenth day in Wiener's case). The extent of the rise, however, seems to have been much greater in this case even when allowance is made for individual differences in the reading of serum titrations. Thus in our case agglutination with B cells could be detected in a dilution of 1/500,000 compared with the figure of 1/512 given by Wiener. Wiener (1941) has recently stated that with the technique that he employs the average isoagglutinin titre is only 16–32. In this laboratory, using the technique referred to above, rather higher figures are obtained (average 64–128). This difference in the normal end-point is insufficient to account for the much greater rise in titre observed in our case. The slow return to a normal level is in accord with Re's observations.

The changes in the anti-A isoagglutinin—a small initial fall followed by a large rise—at first seemed to be a non-specific response to the injection of the group B blood. Then, however, a more convincing explanation suggested itself. At the time when these observations were made, Aubert, Boorman and Dodd, of this laboratory, were engaged in confirming and extending the work of Schiff (1924); an account of their work is in the press. Schiff first demonstrated the presence of the group-specific substances in soluble form in the serum and postulated an equilibrium between the concentration of agglutinogen in erythrocytes and serum. With this fact in mind, it seemed likely that the rise in the titre of the anti-A agglutinin might have been due to the injection of group A substance in either the plasma or serum that

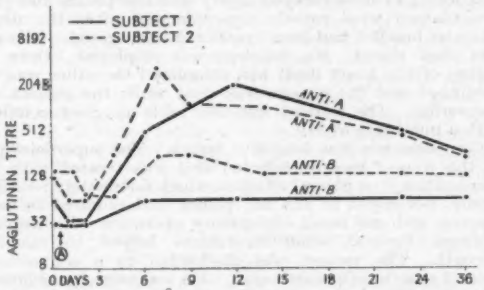



FIG. 3—Control experiments. Changes in titre of anti-A agglutinins in two patients of group O after the transfusion of 100 c.cm. of four-times normal concentrated human serum of group A, reconstituted from the dried product. The serum had been Seitz-filtered before being dried. Transfusions given at A.

had been transfused in the course of treatment. The plasma, however, was taken from a pool of different groups. It has been demonstrated that this plasma is virtually free of agglutinins, and it may therefore be safely assumed that it only contains traces of the corresponding agglutinogens. The serum, on the other hand, was found to be of group A and had not been pooled. Soon after we had made these observations, Aubert and his colleagues demonstrated that it was possible to produce an immune response in man to the agglutinogen contained in serum of groups A, B or AB. This latter work was carried out with Seitz-filtered human serum. Since the serum injected in our case was a four-times concentrated solution, reconstituted from dried serum * which had been Seitz-filtered before drying, we tried the effect of injecting similarly prepared serum of group A into two people of group O. The results are given in fig. 3. As will be seen, after a small fall, the titre of the anti-A agglutinin rose considerably. Thus a satisfactory explanation for the changes in the titre of the anti-A isoagglutinin in the patient who also received group B blood was reached.

It will be noted that the rise in titre of the anti-A isoagglutinin was also very great and considerably exceeds that of the two "controls." It also exceeds that produced by Aubert in any of his experiments (personal communication). The fact that the rise in titre of both agglutinins was so large suggests the possibility of some non-specific stimulation in each case. Aubert has noted slight changes in the anti-A agglutinin after the injection of the B agglutinogen in B serum and vice versa. Further, it is well known that the naturally occurring anti-A or anti-B agglutinin in the serum of some rabbits is often much increased after the injection of OM or ON cells to produce anti-M or anti-N sera. Davidsohn (1938) has pointed out that the isoagglutinin titre of human serum is increased after the induction of serum sickness. In view of these observations it seems reasonable to suppose that some reciprocal non-specific stimulation may have occurred between the one antibody response and the other.

Before this explanation for the changes in titre of the anti-A isoagglutinin had suggested itself, the recipient's serum was tested for the presence of anti-M and N agglutinin, in case their production had been stimulated. No anti-M or anti-N antibodies were found.

As has been mentioned, agglutinates were detected in the recipient's blood-stream up to the seventh day after transfusion. Only until the day after the transfusion, however, were these agglutinates fair-sized. From this day until the seventh only a few small agglutinates persisted, but even on the seventh day a few clumps of five cells were seen. No clumps could be detected on the eighth day or later. Burnham (1930) found some donor cells remaining in the recipient's blood-stream on the third day, but none on the sixth day, after the transfusion of incompatible blood. Wiener and others (1941) in another case found that all but a few of the incompatible cells had been eliminated two days after transfusion.

The rise in serum-bilirubin is a typical finding and is too great to be attributable to the transfusion of stored blood per se. In our experience the transfusion of blood previously stored for three days with a citrate-saline-glucose solution normally leads to only small transient increases in the serum-bilirubin of the recipient.

From the clinical aspect the case adds nothing to existing knowledge of the syndrome of renal insufficiency after the transfusion of incompatible blood, particularly because of the complicating factor of severe injury. As Grant and Reeve (1941) have recently pointed out, there is as yet no precise knowledge of the circumstances in which renal function is disturbed in air-raid casualties.

The passage of many red cells in the urine may have been due to a contusion of the left kidney, since that side of the body was very bruised.

It is interesting to note that there was no immediate reaction to the transfusion—540 c.cm. of citrated stored blood (containing 360 c.cm. whole blood) was transfused in approximately thirty minutes, but no untoward effects were noted. The temperature, however, was not recorded. Others have noted that the transfusion of incompatible blood is not necessarily accompanied by any obvious immediate reaction (Grove and Crum 1930, Wiener and others 1941).

The progress to uræmia and then to recovery was very similar to that of some of the cases described by Bordley (1931), and the final outcome was in close accord with his observation that no patient receiving less than 350 c.cm. of incompatible blood died.

Knowledge of alterations in the titre of the affected agglutinin, after the transfusion of incompatible blood, has important practical applications. First, if after a hæmolytic reaction, cross-matching is repeated with serum obtained from the recipient within a day or two of transfusion, a false negative result may be obtained owing to the temporary suppression of the agglutinin concerned. Secondly, when the donor cannot be traced, serial titrations of the recipient's serum will decide whether or not the blood given contained an incompatible agglutinogen. Thirdly, cross-matching repeated on the

* From the Medical Research Council's serum-drying unit at Cambridge.

tenth to fourteenth day after transfusion is most likely to detect the presence of a weak or atypical incompatible agglutinin, since the immune response will be maximal at this time.

SUMMARY

After the transfusion of group B blood to a woman of group O, changes in the titre of the anti-B isoagglutinin were observed. There was an initial reduction, followed by a rapid increase, and then a slow fall to the original level. These findings confirm previous observations.

Similar changes in the titre of the anti-A isoagglutinin were also found. These changes almost certainly represent a response to the injection of the A agglutinogen contained, in soluble form, in the group A serum transfused in the course of treatment.

We are grateful to the medical officers of the hospital concerned for allowing us access to their patient and to Dr. O. M. Solandt, then director of this depot, for helpful criticism.

REFERENCES

Aubert, E. F., Boorman, K. E. and Dodd, B. E. Personal communication.
Bordley, J. (1931) *Arch. intern. Med.* **47**, 288.
Burnham, L. (1930) *Ibid*, **46**, 502.
Bushby, S. R. M., Hart, E. W., Kekwick, A. and Whitby, L. E. H. (1940) *Lancet*, **1**, 355.
Davidsohn, I. (1938) *Amer. J. clin. Path.* **8**, 179.
Grant, R. T. and Reeve, E. B. (1941) *Brit. med. J.* **2**, 329.
Grove, E. F. and Crum, M. J. (1930) *J. Lab. clin. Med.* **16**, 259.
Rø, J. (1937) *Acta. chir. scand.* **80**, 283.
Schiff, F. (1924) *Klin. Wschr.* **3**, 16.
Taylor, G. L. and Prior, A. M. (1938) *Ann. Eugen.* **8**, 343.
Wiener, A. S. (1939) Blood Groups and Blood Transfusion, Springfield, Ill.
— (1941) *J. Immunol.* **41**, 2, 181.
— Hyman, M. A., Oremland, B. H. and Samwick, A. A. (1941) *Amer. J. clin. Path.* **11**, 2.

# STAB WOUNDS OF THE HEART AND PERICARDIUM

## FOUR CASES WITH THREE RECOVERIES

THEODORE SCHRIRE, M.B. CAPE TOWN, F.R.C.S.
SURGICAL REGISTRAR AT THE GROOTE SCHUUR HOSPITAL, CAPE TOWN

IT has been our practice to explore and do an open thoracotomy on all consenting cases of penetrating wounds of the chest admitted to our beds at the New Somerset and later the Groote Schuur Hospitals. Experiences in a series of 17 cases since the procedure became standardised were detailed in a previous paper (Schrire 1940). In this report 4 cases of penetrating wounds of the pericardium and 2 of perforation of the right ventricle are described.

### WOUND OF THE SURFACE OF LEFT VENTRICLE

CASE 1.—A coloured man, aged 36, was admitted to the New Somerset Hospital on March 26, 1936, with a stab wound of the chest received in a drunken brawl an hour before admission. The knife had entered the left 6th interspace 1 in. outside the nipple line and the wound was bleeding profusely; the patient was cold and breathless. Morphine, gr. ¼, was given immediately and the wound was temporarily plugged with dry gauze. After an hour he had recovered sufficiently from his shock to be operated on. Anæsthesia was induced with chloroform and ether and continued with ether. The wound was excised and the interspace opened up; to increase the exposure, the costochondral cartilages of the 5th and 6th ribs were divided and a rib-retractor was inserted. The lung had escaped injury and a wound, ¼ in. long, was seen in the pericardium over the left auricle; no blood issued from it. The wound was enlarged and it was then possible to see that there was a superficial slit on the surface of the left wall of the left ventricle which had divided the superficial fibres of the myocardium; there was no bleeding from this wound and it was left untouched. Two interrupted sutures were then inserted to close the pericardium and the chest was closed. No drain was used. The patient stood the operation well. His condition was satisfactory till the next day when his pulse-rate began to rise and he died 24 hours after the injury. Autopsy showed that death was due to hæmorrhage from the 6th intercostal artery which had bled into the pleura.

### PENETRATING WOUND OF RIGHT VENTRICLE

CASE 2.—A coloured man, aged 46, was admitted to the New Somerset Hospital on Feb. 27, 1937, having been stabbed with a kitchen knife half an hour before admission. On examination in the casualty department a wound ½ in. long and transverse in direction, was seen 1 in. inside and 1½ in. above the left nipple. He was much shocked. The pulse-rate was 96. A probe inserted into the wound could not be made to enter the thorax. The pulse remained steady for 2 hours; during this time occasional profuse jets of dark blood issued from the wound. Physical examination showed a complete absence of breath sounds and dullness of the left side of the chest. No heart sounds could be heard on the left side: but distant sounds were found behind the lower half of the sternum. With 1% procaine as a local anæsthetic an incision 4 in. long was made in the line of the 5th rib and the small skin wound was excised. The 5th costal cartilage was found to be severed in an oblique direction and 3 in. of it and of the 5th rib were resected. A hole in the pleura about 1½ in. long was found and enlarged. The left lung was seen to be partially collapsed but every now and then the patient would take a deeper breath, or cough, and the lung would be forced into the wound. A slit on the anterior surface of the pericardium was now seen from which dark blood welled up and overflowed into the pleura which contained about a pint. The flow from the pericardium was intermittent, occurring about three times a minute. The wound in the pericardium was enlarged and a hole was found in the right ventricle ½ in. to the right of the anterior interventricular vessels. From the hole in the heart, which was ¾ in. long and transverse in direction, dark blood issued in large jets synchronous with the heart beats. My left forefinger, placed in this wound, controlled the bleeding. I decided to enlarge the opening in the chest wall, and, as the patient would not keep still and the hæmorrhage was under control, open ether was given. Using the right hand, I prolonged the skin vertically downwards for 3 in. along the left border of the sternum and divided the 6th left costal cartilage. The rib-spreader was now introduced and a good view of the pericardium and heart was obtained. A curved needle with no. 1 chromic catgut was now used to put in the first suture through the middle of the cardiac wound and this was tied fairly loosely so as to approximate, but not tear through, the wall of the ventricle. Using this suture as a guy, five more interrupted sutures were inserted and the bleeding was stopped. The pericardium was then closed with three interrupted catgut sutures. The lung was found to have escaped injury and the pleura and chest musculature were rapidly approximated after the neurovascular bundles had been transfixed and ligated. The skin was then closed. No drainage was employed. Once the suture of the heart itself was completed the ether was discontinued and the closure was done while the patient was recovering. The patient left the table in good condition with a pulse-rate of 110.

Convalescence was long and trying. The superficial part of the wound became infected and was treated with hot fomentations; a pleural effusion, which fortunately remained sterile, developed in the left pleura and required frequent tapping and one small exploratory operation with negative findings. Several blood-transfusions helped to maintain strength. The patient was discharged to a convalescent home 3 months after admission. He was seen a year later in good condition and was in full work.

### WOUND OF PERICARDIUM AND PLEURA; CARDIAC TAMPONADE

CASE 3.—A coloured man, aged 21, was admitted drunk to the Groote Schuur Hospital on Oct. 3, 1938. He had been stabbed in the chest an hour before, and was cold, clammy and shocked; the casualty-officer noticed that the pulse was small and rapid and the respirations shallow. The wound, 1 in. from the right border of the sternum in the 5th interspace, did not bleed to any unusual extent. Under observation, the pulse became imperceptible and his general condition steadily deteriorated while the apex-beat was neither visible nor palpable. Cardiac tamponade was diagnosed and the patient was operated on an hour after admission. He was wildly excited and quite uncoöperative, and anæsthesia was induced with $C_2E_2$ and maintained with nitrous oxide, oxygen and ether. The chest was opened by a vertical incision which ran parallel and 1 in. lateral to the right border of the sternum, and the original wound was excised. Three costal cartilages were resected to improve the exposure. There was some blood in the pleural space, but owing to dense old adhesions the lung had not retracted and it was necessary to separate the adhesions by means of sharp dissection in order to get a working space; the internal mammary artery was

divided between ligatures. There was no wound in the lung and the pericardium was now inspected—it was tense and blue—cardiac pulsations were only barely palpable on its surface and no wound could be found. An exploring needle was inserted and blood was withdrawn. The pericardium was accordingly opened and about ½ pint of blood escaped with a rush; the anæsthetist immediately reported a considerable improvement in the quality of the pulse and the heart could be seen beating freely. In spite of careful search no bleeding point could be seen on the surface of the heart or on the pericardial walls and it was decided to close the chest. The pericardium, incised as it was for about 3 in., was left wide open and the pleura was drained. The chest was now closed. One pint of blood was given on the patient's return to the ward.

The next day the man's condition was fairly good, but his mental state was unsatisfactory. About 10 oz. of blood-stained fluid had drained from the tube when the patient pulled it out and it could not be reintroduced. Repeated aspirations were done and a fortnight later an empyema was drained under local anæsthesia. By the end of October the patient was in a poor way; he had air-hunger, his respirations were laboured, the temperature was swinging and the pulse-rate was 140. Radiography showed the pericardial shadow to be greatly enlarged in all diameters, and on screening restricted cardiac pulsations were seen. A diagnosis of suppurative pericarditis was made. On Oct. 29, 1938, pericardiotomy was done under local anæsthesia. An incision 3 in. long and parallel with the left lower border of the chest was made, beginning at the chondroxiphoid junction and extending downwards and laterally. The 7th left costal cartilage was removed and the perichondrium deep to it cut away. This exposed the internal mammary artery which was divided between ligatures. Dissection was carried out in the chondroxiphoid angle and the surface of the pericardium, tense and pale, was found. Owing to the position of the incision there was no risk of damage to the left pleura. The pericardium was opened and a profuse flow of thick pus came out in jets synchronous with the heart beat. A finger was inserted into the pericardium and "bread-and-butter" adhesions, such as can be found in old empyemata, were felt and separated; more pus escaped. A drainage-tube was placed down to the pericardium and the patient was nursed sitting upright to facilitate drainage; 2 pints of blood were given immediately. Saline irrigations carried out twice daily allowed a profuse discharge of pus to escape. The temperature settled and the general condition improved. A pure streptococcal culture was obtained from the pus and sulphanilamide was given to control the infection. The patient was discharged to a convalescent home on Dec. 14, 1938. On Nov. 8, 1939, he returned for incision of an abscess at the site of the original wound. This cleared up without any trouble. He had been on full work for the last 8 months as a packer in a furniture factory and had noticed no ill effects as a result of his pericarditis.

### THORACO-ABDOMINAL WOUND PENETRATING THE RIGHT VENTRICLE

CASE 4.—A coloured man, aged 25, was admitted on Nov. 12, 1938, to the Groote Schuur Hospital suffering from a stab wound in the left side of the chest, through which 3 in. of omentum projected. It was thus evidently a thoraco-abdominal injury. The patient was in good condition and operation was undertaken 2 hours after admission. Under open ether anæsthesia, an incision in the 7th interspace about 10 in. long with its centre surrounding and excising the original stab, which was in the mid-axillary line, was made. The chest was opened and the neurovascular bundle beneath the 7th rib was tied off after it had been under-run. A rib-spreader was introduced and the hole in the diaphragm identified. This was about 3 in. long; the spleen could be seen just under the hole. A moderate amount of blood in the pleural cavity was mopped up and the lung was pulled down, examined, and being uninjured was released and allowed to retract. At this point it was noticed that the pleura had once more filled with blood, and this was traced to a wound about ½ in. long on the posterior surface of the pericardium. The pericardium was then seen to be tightly distended with blood. Since it was now obvious that a cardiac wound was present I decided to close the diaphragm and not to explore the abdomen further. The omentum was returned to the abdomen and the diaphragm was sutured with two layers of continuous no. 2 chromic catgut. The left phrenic nerve was crushed as it passed over the pericardium to paralyse the diaphragm and facilitate subsequent manipulations. The rib-spreader was now removed and another incision, at right angles to the first, was made extending for about 4 in. upwards and inwards; this gave an inverted T-shaped incision. The 7th, 6th and 5th ribs were cut in the line of the supplementary incision, and their neurovascular bundles divided between ligatures; it was now possible by means of strong traction to elevate a sort of flap consisting of the chest wall, upwards and outwards. The rib-spreader was reintroduced. The pericardium was now opened and about ½ pint of blood escaped. The heart was delivered into the wound, but owing to its movements it was impossible to reach its posterior surface. A no. 2 chromic suture was passed through the fibro-fatty tissue at the apex and this acting as a tractor, the heart was lifted out and its posterior surface exposed. A wound about ½ in. long was found on the posterior surface of the right ventricle, close to the posterior interventricular vessels and about a third of the distance between the auriculoventricular sulcus and the apex. Two sutures of no. 1 chromic were inserted and these controlled the bleeding. The traction suture was now cut, the heart returned to its place and the pericardium was left wide open. A stab wound was made in the 8th space posteriorly and a self-retaining catheter was inserted. The chest wound was then closed and the patient returned to bed.

Convalescence was uneventful. The tube was removed in 48 hours and the patient left the hospital at his own request on Dec. 2, 1938. When seen 2 months later he was fit and at work again as a labourer.

### DISCUSSION

These cases show variable symptomatology. Thus, 3 were shocked on admission; the fourth, who had the thoraco-abdominal wound, was in good condition. It will be noticed that case 2, though apparently shocked on arrival at hospital, had a pulse-rate of 96 which had risen to 110 on leaving the operating table. Only in cases 1 and 2 was there any profuse external bleeding, which in case 2 came in occasional jets of dark blood; this patient had a penetrating wound of the right ventricle. In the other case of right ventricular penetration (case 4) external bleeding was not noteworthy. In case 2 the heart was saved from pressure by leakage into the pleura. Cardiac tamponade, characterised by a rapid pulse of decreasing volume with absence of an apex-beat, occurred in only one patient (case 3) in spite of the fact that the pericardium communicated with the pleural cavity; here, old adhesions seem to have prevented leakage of blood into pleura.

Every case was explored along the track of the wound. The original skin incision was excised and the wounded interspace widely opened; a view of the damage was then obtained, regardless of chest-wall structures. Ribs were sectioned with shears, costal cartilages were divided with a knife and—except in case 1—interspaces were cut across between two ligatures which transfixed and tied the neurovascular bundles. The importance of this last procedure is measured by the fact that the only death in the series (case 1) was due to a leaking intercostal vessel.

In order to suture the penetrating heart-wounds in cases 2 and 4 it was necessary to steady the heart. In case 2, a finger was placed in the hole in the heart (Elkin's manœuvre 1936). In case 4, where the stab pierced the phrenic surface of the right ventricle, a suture was passed through the fibro-fatty tissue at the apex and used as a tractor to lift the heart (Beck 1926). The chest was closed quickly by bringing the ribs together with pericostal sutures. Intercostal muscles were disregarded but parietal layers were carefully closed.

Separate drainage of the pericardium invites ascending infection. It is better to leave the pericardium opening widely into the pleural cavity and to drain the pleura with a large self-retaining catheter passed into the chest through a cannula; the end of the catheter dips under water. It is possible to get a wound of the heart without penetration of the pleura (Elkin and Phillips 1931), but even in such cases it would usually be necessary to open the left pleura in order to get sufficient exposure; so that pleural drainage would entail little extra structural damage. If case 2 had been drained, the patient might have been saved many tappings and an exploratory thoracotomy. In casé 3 the adhesions appear to have prevented satisfactory pericardiopleural drainage.

Search of the literature has shown only 10 cases of thoraco-abdomino-cardiac wounds with 2 recoveries, both recorded by Pool (1912). Case 4 is a third instance of recovery after this rare lesion.

I am indebted to my chief, Mr. W. L. Gordon, F.R.C.S., for permission to use his beds and for moral support, and to Dr. G. A. Elliot, Dr. Arthur Landau and Prof. J. F. Brock for assisting in the after-treatment of the cases.

REFERENCES

Beck, C. S. (1926) *Arch. Surg. Chicago*, **13**, 205.
Elkin, D. C. (1936) *J. thorac. Surg.* **5**, 590.
— and Phillips, H. S. (1931) *Ibid.* **1**, 113.
Pool, E. H. (1912) *Ann. Surg.* **55**, 485.
Schrire, T. (1940) *Brit. med. J.* **2**, 662.

## Reviews of Books

### Lymphatics, Lymph and Lymphoid Tissue

*Their Physiological and Clinical Significance.* C. K. DRINKER, M.D., D.Sc., professor of physiology, school of public health, Harvard University; and J. M. YOFFEY, M.D., F.R.C.S., senior lecturer in anatomy, University College of South Wales and Monmouthshire. Cambridge, Mass: Harvard University Press. Pp. 406. $4.00.

THIS book, appearing at a time when the behaviour of the lymphatics is exciting a good deal of attention, records what is known and indicates what is yet unknown about the lymph and the lymphoid tissue. The first half of the book describes the composition, formation and circulation of the lymph. It seems clear that, while proteins and particles, including bacteria, may escape from the blood capillaries together with fluid carrying solutes, only solutes with variable amounts of fluid can return again through the capillary wall. Protein molecules and particles, with the remainder of the fluid, must make their way back to the circulation by the lymphatics. The conditions governing capillary permeability under normal and pathological conditions are discussed, and there is a detailed account of the lymph flow from the various parts of the body. It seems that much is known about the lymph flow from some organs and regions of the body and hardly anything about the flow from others. Much work on lymph flow has been done in Professor Drinker's own laboratory.

Experiments have resulted in lymph being obtained from several of the less accessible parts of the body. In connective tissues the lymphatics seem to be relatively permeable, particles and proteins entering them with ease and rapidity. From mucous and serous surfaces, fluids and the smaller protein molecules readily enter the lymphatics, whereas the larger proteins and particles as a rule do so only very slowly. Absorption from the nasal cavity has been studied in great detail, and an account is given of the passage of virulent bacteria and viruses from the nasal mucosa into the cervical lymph. The authors think it almost certain that substances will only pass through the cribriform plate from within outwards. They believe that the lymph, and in particular the lymphocytes, may play an important part in the dissemination of viruses throughout the body. Although the vaccinia virus, which is pathogenic for rabbits, can be isolated from the cervical lymphatics soon after instillation into the animal's nose, it is apparently impossible to detect the virus of poliomyelitis in the lymph after it has been dropped into the nasal cavities of monkeys.

Factors controlling the flow of lymph are discussed at length. In the limbs, at any rate, the flow is more or less independent of the production of lymph; the formation of lymph depends on capillary permeability, but the removal from the tissues of the fluid so extruded depends almost entirely on extrinsic factors such as movement, massage and posture. The authors maintain that lymph and tissue fluid are identical; but it is not clear how much of the fluid actually exists free among the tissues.

The second part of the book reviews the many theories which have been brought forward to explain the functions of lymphocytes and lymphoid tissue. The mystery remains complete, but the summary of a very extensive literature is an able one. It is interesting to learn that phylogenetically the lymphoid tissue has quite a separate origin from the lymphatic vessels. The authors go to some lengths to emphasise their belief that the lymphatics play a very small part in the reduction of œdema in the limbs. It is difficult to agree with them since, as they point out, it has been clearly shown that the lymphatics in œdematous areas are held widely open; thus the flow of lymph along them would be greatly augmented by movements and pressure so slight as to produce little increase of flow in a normal limb. Again, the reader is not left with a clear idea of the view the authors take about the part played by the lymphatics in the body's fight against infection.

### Sick Children

(4th ed.) DONALD PATERSON, M.D. Edin., F.R.C.P. London: Cassell and Co. Pp. 610. 15*s*.

THIS is one of the smaller handbooks of children's diseases, but it is unusually comprehensive. To take two examples: mental tests suitable for various ages are printed in an appendix; and there is a set of radiograms showing the ossification of the wrist and hand from birth to the age of fifteen. The index is fairly good and the illustrations are excellent. A number of items are frankly abstracts, references to the originals being faithfully given; and the effect of authenticity thus produced is maintained by the practical tone of the whole book.

### Textbook of the Practice of Medicine

(6th ed.) Editor: FREDERICK W. PRICE, M.D. Edin., F.R.C.P. London: Humphrey Milford, Oxford University Press. Pp. 2032. 38*s*.

AFTER many war-time vicissitudes the new edition of this well-established textbook has at last appeared. Revision, though widespread and on the whole adequate, has been mainly in detail; such innovations as the sulphonamide group, the newer insulins, chest-leads in electrocardiography, and rupture of the intervertebral disc have been introduced. The two war years which have elapsed since the last edition appeared have witnessed comparatively few advances in medicine, but it is somewhat surprising to find no reference to the medical aspects of poison gases or of shock, and a section on military medicine would not have been out of place. More space is allotted to visceroptosis than to either carcinoma of the stomach or jaundice and the Meulengracht diet is dismissed in a few scathing words. The section on diabetes mellitus is more likely to confuse than enlighten the reader, and perhaps the editor should have made it clearer that his own views on primary cardiac strain are unorthodox. Of the 99 illustrations all but 22 (of which at least 2 could have been spared) fall in one section. These are minor criticisms and the new edition is well representative of the teaching of the London medical schools.

### Second Yearbook of Research and Statistical Methodology

Editor: O. K. BUROS. New Jersey: The Gryphon Press. Pp. 383. $5.

IN this second venture, which in minor ways is a great improvement on the first, the editor lists 359 books, written in English and published since 1933, which deal with statistical methods, scientific methods, social relations of science and similar subjects, together with selections from the published reviews of them. Any such list is clearly helpful to the research worker, the teacher and the taught, but the value of "evaluative comments" contained in reviews is open to some doubt, reviews of the same book being often laudatory, derogatory or vacuous according to the school of the reviewer. Many reviews deserve no further publicity than they originally received, though Mr. Buros rather optimistically hopes that his reproduction of them will stimulate editors and reviewers to do better. Given sufficient help and money he would like to extend his field to books in other languages and to non-critical and critical abstracts of the literature on research and statistical methodology. This might be of greater benefit to interested workers than the present pages of extracts from many reviews of the same book. Incidentally, the index of names leaves much to be desired, the page reference being to the book listed. Mr. A., therefore, is mentioned in connexion with book no. 20, but since references to book no. 20 occupy 11¼ pages it takes Mr. A. some time to learn what is said of him or what he said of it.

# Cardophylin

(THEOPHYLLINE-ETHYLENEDIAMINE)
= EUPHYLLIN

## AN IMPROVED PURIN DERIVATIVE

The important place which purin compounds occupy in therapeutics is especially manifested during this period of restricted supplies.

CARDOPHYLIN, which contains approximately 78 per cent. of Theophylline in a soluble and greatly improved form, is readily obtainable. A powerful vaso-dilator, diuretic and respiratory stimulant, CARDOPHYLIN is indicated in the treatment of

- ANGINA PECTORIS
- CHEYNE-STOKES BREATHING
- CARDIAC and BRONCHIAL ASTHMA
- ARTERIO-SCLEROSIS
- MYOCARDIAL DEGENERATION
- ŒDEMA, etc.

*In tablets, ampoules and suppositories*

Literature and samples on request

**WHIFFEN & SONS, LTD.**

Carnwath Road, London, S.W.6

*Tel.: FULham 0037*

# A *Natural* TONIC WINE that may be prescribed with every confidence

Because of its freedom from drugs, Tintara may be prescribed with every confidence in all cases where a Tonic Wine is indicated. Tintara is an Australian Burgundy of exceptionally robust character, produced on ferruginous soil. It is a well-balanced wine of minimum acidity. It contains no added alcohol, no sugar. It is a pure natural product from the Empire's most famous vineyards.

IN FLAGONS & ½ FLAGONS

A flagon equals a bottle and a half

Also in BOTTLES & ½ BOTTLES

# BURGOYNE'S TINTARA

*pure* TONIC BURGUNDY

*A sample will be gladly sent free in the United Kingdom on receipt of professional card*

**P. B. BURGOYNE & CO., LTD.**

DOWGATE HILL, LONDON, E.C.4

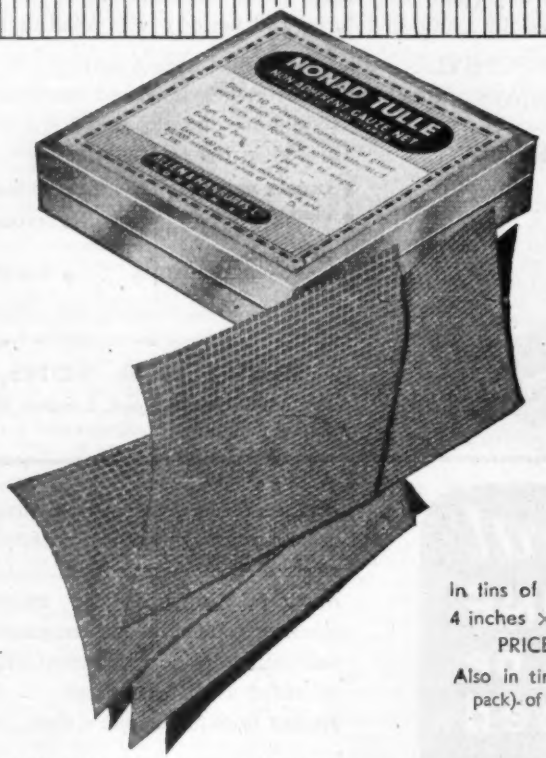
*Telephone CITy 1616*

# NONAD TULLE

TRADE MARK

## NON-ADHERENT GAUZE NET

VITAMINIZED & STERILIZED




In tins of 10 pieces,
4 inches × 4 inches
PRICE 3/6
Also in tins (Hospital pack) of 30 pieces

NONAD TULLE is a gauze with a mesh of 2 millimetres and impregnated with 98 parts of soft paraffin, 1 of balsam of Peru, and 1 of halibut-liver oil, that rich source of Vitamins A and D.

Dressings made with NONAD TULLE as their foundation are easily removed, without pain or bleeding. Through the wide mesh, secretions are easily absorbed by the outer dressings: accordingly dangerous products do not accumulate in the lesion, and it need not be dressed so often as usual.

NONAD TULLE may be used on septic wounds, burns, gangrene, sloughs, varicose ulcers, indolent wounds, operation wounds, pruritic or infective eruptions, and solar or actinic dermatitis.

**NONAD TULLE PROMOTES QUICK HEALING**

ALLEN & HANBURYS LTD., LONDON, E.2

*PHONE:* BISHOPSGATE 3201 (12 lines). *WIRES:* "GREENBURYS, BETH, LONDON"

THE LANCET

*LONDON: SATURDAY, NOVEMBER 22, 1941*

## REST FOR INFLAMED TISSUES

NATURE'S method of healing has never altered; it is our technique of how to assist her that changes. Rest has always been the most natural ally of the vis medicatrix naturæ on which all healing depends. A long line of "Menders of the Maimed" in British medicine—HUNTER, HILTON, HUGH OWEN THOMAS and others—taught that inflamed tissue is capable of dealing with its enemies unaided if kept at rest. But there are varying degrees of rest. To lie in bed does not necessarily keep the whole body at rest, the many splints are not always effective, and any fixation by traction will exert a pull on diseased structures. There is no doubt, however, that strict local rest of the injured part is obtained by the closed-plaster treatment of infected wounds. THOMAS and many others would not use plaster because they felt that it impeded the circulation in the diseased part. But a properly applied plaster supports rather than constricts the vessels of supply. The comfort of the patient in plaster is our surest proof. Muscles are tissues with high vascular demands, and, as we know from Volkmann's contracture, when there is compression of the main vessel the muscle will die long before there is skin involvement, and any shortage in its blood-supply is soon demonstrated by exquisite pain. In the resting limb the maximal blood-flow is determined to a great extent by the diameter of the larger supplying arteries. A good blood-supply, and therefore an intact major vessel, is the sine qua non of the closed-plaster method of treatment. As TRUETA has urged, if the blood-supply of the limb is jeopardised either by trauma or operation, treatment in closed plaster is to be avoided. A trickling stream will provide special opportunities for the flourishing of organisms, especially anaerobic, and against these early operative interference is our most useful aid.

The theoretical basis of the closed-plaster treatment is by no means fully understood. Exactly how does a plaster prevent the spread of infection? SAMPSON GAMGEE believed that pressure on a wound directly benefits the development of the cells in it by preventing degeneration and vacuolation; WINNETT ORR ascribed a special virtue to the soft paraffin with which he packed the wound; ALBEE suggested that bacteriophage is produced under the plaster; and GARCIA ALONSO maintained that a sort of civil war among the various types of bacteria confined under the plaster prevents the domination of pyogenic organisms. Probably all these views hold something of truth, but the experimental work of BARNES and TRUETA [1] offers the most likely explanation of the success of complete immobilisation. The flow of the lymph is the clue. It has long been known that the capillary endothelium of the blood-vessels is resistant to bacteria and that infection reaches the blood-stream via the lymphatic circulation. Anything that diminishes the flow in this lymph will therefore help to localise the infection, and DRINKER showed and BARNES and TRUETA have confirmed that if a limb is immobilised the flow of lymph almost ceases. It apparently does not cease completely, for, as CRESSMAN and BLALOCK [2] point out, transmitted arterial pulsations probably produce some slight movement of lymph. This movement CLARK and CLARK [3] describe as a "bobbing" back and forth synchronous with the heart beat or respiration, with only a sluggish forward movement. Besides the lymph-trunks, which via the glands lead to the blood-stream, the lymphatic system consists of a network of anastomosing, interlacing vessels. Thus, if there is movement, not only does the lymph carry bacteria to the lymph filters, and on rare occasions to the blood, but local spread takes place because infection is squeezed into the lymphatic meshwork. BARNES and TRUETA demonstrated experimentally that manual compression of the muscles produces no increased flow in the lymph-trunks but that full joint movement does greatly increase the flow. Hence the importance of immobilising the joints above and below an infected wound. Immobilisation has, of course, other important functions. It protects the frail capillary endothelium, which tears readily and waits with pouting mouths for further organisms. A dressing with the gentlest hands is then like the tramplings of an elephant's feet. GAMGEE knew the importance of support for tissues which through bruising, incision or œdema have lost their natural elastic support. DICKSON WRIGHT taught the same in the treatment of varicose ulceration, where he showed that lack of support interfered with the blood-flow and that even pressure was the surest way to get the best blood-supply and healing. WINNETT ORR recognised the fragility of capillary endothelium and that is why he recommended soft paraffin. TRUETA realised that, provided the limb was at rest, a multiplicity of organisms disporting themselves on the wound surface interfered but little with wound healing.

There has always been the fear of ankylosis of the associated joints when immobilisation is prolonged. For acutely inflamed joints it was even the habit in the last war to insist on the patient moving despite the exquisite pain. Over fifty years ago THOMAS condemned this practice in a forcible manner when he wrote: "it is as reasonable to attempt to cure a fever patient by kicking him out of bed as to benefit joint disease by wriggling at the articulation." OGILVIE [4] has said the same in discussing the treatment of wounds and sepsis of the knee-joint. He maintains that immobilisation must be continued until infection is clinically overcome, and that the joint must therefore be completely immobilised for a minimum of three weeks. The slightest movement, such as changing a plaster, will result in a flare-up, and to immobilise a knee-joint absolutely nothing less than a hip spica will do. To stretch damaged or healing tissues by early movements does not loosen them but actually results in the laying down of more and more scar tissue in the lines of strain. Where it is particularly important to avoid scar formation, as in septic

1. Barnes, J. M. and Trueta, J. *Lancet*, 1941, **1**, 623.

2. Cressman, R. D. and Blalock, A. *Proc. Soc. exp. Biol. N.Y.*, 1939, **41**, 140.
3. Clark, E. R. and Clark, E. L. *Amer. J. Anat.* 1932, **49**, 441.
4. Ogilvie, W. H. *Lancet*, 1941, **1**, 471.

burns, immobilisation in plaster is being used to keep the healing tissues at rest; and in the deep burn it also enables a barrier of granulations to develop which seals off important structures such as tendons and joints.

In the early stage of acute sepsis, except when there is lymphangitis, the use of closed plaster to secure the essential strict immobilisation does not seem desirable. In the closed progressive acute lesion, where pus has still to be evacuated, the closed plaster will increase the tension in the tissues walling the forming abscess and is thus to be avoided. The time for plaster only begins when effective drainage has been established. The experimental work of TRUETA and BARNES shows that only in the draining, inflammatory limb will plaster cause the lymph flow to cease. In the early stage of acute sepsis, therefore, strict immobilisation of the joints above and below by splintage, either by plaster slab or other material, is called for. As soon as drainage is established the closed-plaster method can be applied. As in wounds of war the closed-plaster method is for the open draining wound. FRASER [5] has used this method in the treatment of acute osteitis, where after drilling the bone, as advocated by STARR, he packed the wound and encased it in plaster. DODD [6] insists on strict immobilisation in the treatment of multiple boils. He thinks that any movement —squeezing, bathing or fomenting—may detach infected thrombi which may settle in the skin, or may form abscesses in the kidney, ischiorectal fossa or bone. He therefore confines the patient to bed, securing rest by infrequent dressings, and by splinting (even for boils of the neck, where he uses a long back splint with foot piece for the head) and his results have been gratifying. He also [7] advocates complete rest in the management of abdominal distension after operations on the gut, and most surgeons would agree that immobilisation is the principle to be followed in all forms of intra-abdominal inflammation, though they might differ as to the method by which rest is best secured—for instance, when and in what dosage should morphia be given? In the treatment of infected fingers there has also been difference of opinion about the value of immobilisation. As JEAN PIERRE DAVID of Rouen wrote in 1779: "there is a time for rest and a time for motion in the treatment of most surgical conditions." Those who use plaster for wounded fingers hold that complete rest for two or three weeks does not lead to stiffness, and longer periods are harmless if the position of the fingers is changed once a fortnight. When the inflammation has subsided, they say, and there is no risk of tearing capillaries or spreading infection, movement should begin.

Nevertheless in all these cases the disadvantages of immobilisation, especially if long continued, must be recognised, the inconvenience of the patient must be considered and a balanced outlook maintained. The theoretical foundations of the principle of complete rest have been established, and in this war its application to infected wounds has been brilliantly successful; it still remains to extend its use and define its indications for the treatment of other infections.

5. Fraser, J. *Ibid*, 1934, 2, 272. 6. Dodd, H. *Ibid*, 1941, 1, 558. 7. *Ibid*, 1940, 2, 98.

## THE HAY-BOX REDIVIVUS

SINCE the beginning of this century the hay-box has enjoyed a deserved reputation among connoisseurs of cookery, and also among lazy amateur cooks who prefer other activities to standing over the cooking stove. It is well known that cooking is possible below the boiling point of water. Indeed it is doubtful if the interior of a roast joint ever reaches such a temperature. The juiciness, palatability and digestibility of the inner cuts are largely due to this fact. Many high-class restaurants use the plan of raising the temperature of the outside of their joints to a high point for a short time in the oven and then removing them to a place where the temperature is lower, so that cooking may continue slowly for a considerable time. This not only produces a more tender cut but is economical in that not so much of the juices of the meat are lost to the exterior. Cooking is much slower by these means, but much less attention is needed after the initial stage, and where time is of little consideration slowness is no disadvantage. A similar principle underlies the cooking of food in a hay-box. Food is brought to the boiling point and then after a few minutes' exposure to that temperature is transferred in its container to a heat-insulated box and left for hours to cook in its residual heat. For many years there have been on the market "fireless cookers" which work on this principle. Foods are boiled in highly polished saucepans, which, when their contents are hot throughout, are removed, tightly sealed, to a metal-lined container into which the saucepans fit snugly. This container is insulated from heat loss by a packing of kapok, asbestos or some other non-conductor of heat. Some hours later, when the container is opened, the food is found to be admirably cooked and may still be smoking hot and ready to serve. An amateur apparatus can easily be constructed from a packing case with hay as the non-conductor, using a weighted cushion also stuffed tightly with hay as a lid. Hence comes the term "hay-box cookery" for all such methods of preparing food for the table.

Hay-box cookery comes to the fore in war-time. It saves fuel. It needs little attention. It releases a person for other duties. When, as at present, married women are at work on munitions, it may solve the problem of the hot meal on the return home at the end of the shift. Also foods can be cooked overnight so that little preparation is needed in the morning before an early start for the works. Earnest amateurs therefore rush in to instruct the working-classes in hay-box cookery, and this naturally arouses the inhibitory instinct of other earnest amateurs who ask "What about killing (sic) the vitamins?". The hay-box has sundry disadvantages. The home-made apparatus is not easy to make or to keep sweet and there is a considerable destruction of vitamin C varying with the length of time the foods remain in the box. Experiments on brussels sprouts, kale and potatoes show a diminution which in the two last named is really serious. Brussels sprouts, with 123 mg. per 100 g. in the raw state have this reduced to 66 after boiling for 15 minutes. Two hours cooking in the box, after this, reduces the amount to 29 and six hours to 24. The sprouts have thus lost two-thirds of their original content, though even so they are still a valuable source of vitamin C. The potato,

starting with 13–27 mg. per 100 g., has this amount reduced to 1 or 2 mg.—a worthless amount. Kale suffers a reduction from 155 mg. to 7, this making it almost useless as a source of vitamin C, though still valuable for vitamin A and probably for calcium and iron. There can be little doubt that similar facts would be discovered with other sources of vitamin C such as swedes, turnips and spinach.

None the less, the hay-box used with discretion is an extremely valuable addition to cooking appliances even in peace-time and may be invaluable in war-time. It will cook most vegetables, stews, meats for boiling, and most cereals and milk puddings, though it is not very successful with rice. And foods left to cook in it are usually hot even after a lapse of 6 hours, depending on the efficiency of the heat insulation and the initial volume of the food. The discretion necessary can be taught and learnt unfortunately only by those with a modicum of dietetics and a knowledge of where to turn for information. It is a gross pity that there is a dearth of trained dietitians to educate the public in hay-box and other cookery, and that, though the need has been outspoken for the last decade and more especially since the war began, little or nothing has been done by any ministry or public educational body to supply such teachers.

## IMMUNITY TO TETANUS

TETANUS is, like gas gangrene, a rare infection in civil practice; both need the opportunity of wounds peculiar to warfare if they are to flourish. The deep penetrating wound soiled by infected earth or clothing and left unattended for twenty-four hours or more provides the ideal conditions for the anaerobic growth of *Clostridium tetani*, and it was only when such wounds were surgically excised and the patient given prophylactic tetanus antitoxin that the incidence of tetanus in the 1914–18 war was reduced from 8–9 per 1000 to less than 1 per 1000. Since then, active immunisation with tetanus toxoid has passed from the experimental stage and the protection of army horses against lockjaw to its clinical application for the protection of the armed forces. BOYD[1] showed that immunity to tetanus, taking 0·01 unit of antitoxin per c.cm. as the effective lower limit, could best be obtained by giving two injections each of 1 c.cm. of tetanus toxoid at an interval of not less than six weeks. The injections produce little or no upset; the only undesirable complication is the rare occurrence of an anaphylactoid reaction after the second dose, apparently due to a protein derivative in the culture-medium,[2] and readily countered by an injection of adrenaline. That this risk is very rare is borne out by the absence of systemic reaction noted by PESHKIN[3] in the immunisation with alum-precipitated diphtheria and tetanus toxoid of 186 allergic children.

The efficacy of BOYD'S method of immunisation was largely substantiated by the absence of tetanus among the 80% or so of the B.E.F. in France who were actively immunised, for circumstances prevented a large proportion of the wounded from getting in addition the recommended dose of tetanus antitoxin[4]; yet cases of tetanus were reported only among those who were not actively immunised. Confirmation of BOYD'S preliminary work has lately come from two sources in this country. MARVELL and PARISH,[5] who recommended intramuscular rather than subcutaneous injection, found that in 116 persons given two 1 c.cm. doses of tetanus toxoid at an average interval of six weeks the titre was less than 0·01 unit per c.cm. in only 13 out of 187 blood-samples tested at intervals ranging from one to nine months after the second injection; 11 of these 13 samples were examined six to nine months after the second dose. It was noted that women responded better to immunisation than men, whereas staff (stablemen and technicians in the tetanus laboratory) whose work might bring them into contact with tetanus toxin gave no better response than other male staff. Those with low titres after the second dose were given a third "boosting" dose which was most effective in raising the titre if given after a long interval (seven to nine months); PESHKIN noted the same phenomenon among his immunised children. These findings have been substantially corroborated by EVANS. On another page he records an investigation of blood-samples from staff of the National Institute for Medical Research who were given two doses of tetanus toxoid at an interval of nine weeks. While none of 81 subjects had 0·01 unit of antitoxin per c.cm. before the first injection, nine weeks later a fifth of them developed more than 0·1 unit in response to the first dose, which suggests that some of them already had a low basal immunity. The second injection brought every person above the 0·01 threshold, and the level of immunity noted seventeen weeks after this dose was largely maintained ten months later; MARVELL and PARISH, and PESHKIN, on the other hand, noted a waning immunity in a proportion of cases with the lapse of time. Like them, EVANS found that a third dose given after an interval of ten months produced a striking rise in titre. Thus, the "injection de rappel" of the French, given a year or so after primary immunisation, has much to recommend it, for it boosts up an already existing immunity and gives the necessary additional stimulus to those few people who do not respond to the first injections. An alternative, and apparently effective, method of immunisation against tetanus is that recommended by RAMON and lately supported by MACLEAN and HOLT[6]—the combination of tetanus toxoid with T.A.B. vaccine in two doses given at a month's interval. With this combination the immediate antibody response to the tetanus toxoid was much greater than when toxoid was used alone, but the subjects were not followed up to find if the immunity was maintained. Another point which is still at issue is whether it is better to give a wounded and immunised man a further injection of toxoid, as French and American authorities advise, or a dose of tetanus antitoxin as is the recommendation of our Army Medical Service. It is conceivable that in a shocked and unattended soldier infected with *Cl. tetani* the sudden liberation into the circulation of toxin accumulated at the site of injury might do irreparable damage before the host's protective mechanism could be stimulated to produce antibody; in such cases artificial antibody seems desirable. Where infection occurs in a healthy non-shocked person, the toxin produced in situ should provide the necessary stimulus without artificial aid from outside.

1. Boyd, J. S. K. *J. R. Army med. Cps*, 1938, **70**, 289.
2. Parish, H. J. and Oakley, C. L. *Brit. med. J.* 1940, **1**, 294.
3. Peshkin, M. M. *Amer. J. Dis. Child.* 1941, **62**, 9, 309.
4. Perry, H. M. *Brit. med. J.* 1940, **2**, 364.
5. Marvell D. M. and Parrish, H. J. *Ibid*, 1940, **2**, 891.
6. MacLean, I. H. and Holt, L. B. *Lancet*, 1940, **2**, 581.

## Annotations

### A MINISTRY OF MEDICAL SERVICES

THE demand for a reorganisation of our medical and health services grows increasingly vocal, the latest exposition being contained in a booklet[1] published by the British Association for Labour Legislation, and written by Dame Janet Campbell and Dr. H. M. Vernon, both of whom have long experience of public administration as well as of clinical work. Written mainly for the lay public, the greater part of the book is occupied by a summary of the recognised merits and defects of the health services as they exist and function at present—facts with which most medical readers are now familiar. The authors agree that the main object to be borne in mind in reconstructing our medical services is to secure, for every man, woman and child in proportion to their several needs, all the medical skill, knowledge and institutional amenities available, independently of individual ability to pay for them. As to method, Dame Janet Campbell apparently favours a great extension and expansion of the panel service: first because it is a system in being; and secondly because it goes a long way towards satisfying the democratic case for freedom of choice. She would also make it include necessary consultant, specialist and hospital services. The approved societies would cease to have any connexion with the medical services, beyond accepting the doctor's certificate of sickness and incapacity—though, as a matter of fact, apart from what are now called extra benefits, there is little other connexion at the present time. But the novel suggestion of the booklet is that the medical and nursing services should be altogether dissociated from the Ministry of Health, a new "Ministry of Medical and Nursing and Social Services" being set up to organise post-war medical reconstruction. It may well be doubted, however, if it would be wise from a national point of view, or in the long run from the narrower point of view of the profession, to dissociate doctoring and nursing from other organised state activities which, we are coming to realise, have a direct bearing on national and personal health.

### SURGERY FOR SYRINGOMYELIA

WHEN the nature of a disease is imperfectly known the response to various forms of treatment carried out more or less empirically must be the principal guide to its management. For this reason the paper in which Worster-Drought, Wakeley and Shafar[2] record their experience of surgical treatment in ten cases of syringomyelia is of considerable importance. There are two good reasons for operation when cavitation causes distension of the cord so gross as to block the subarachnoid space. One is that the pressure on the long tracts in the cord can be most effectively relieved by draining the cavity; the other is the possibility that the signs and symptoms may be due not to a syringomyelic cavity but to an intramedullary tumour. It must be recognised, however, that cavitation rarely progresses to this extent—in the present series, for example, only one out of the ten cases showed signs of a subarachnoid block, though it may be added that, as one might expect, considerable improvement followed operation in this case. Three other patients, however, derived similar benefit from the opening up of cavities which had neither obstructed the subarachnoid space nor produced symptoms in the legs, though changes in the reflexes did indicate some interference with the long tracts. Under such circumstances the permanent clinical manifestations must be due to local destruction of the cord, while the signs which clear up after the cavity has been drained may be attributable to œdema and vascular changes in its immediate neighbourhood. These changes seem to be caused by the pressure within the cavity, which Worster-Drought and his colleagues consider the most important factor influencing the response to surgical treatment. This pressure does not necessarily vary directly with the size of the cavity, but should it be low little can be expected from operation, since signs and symptoms then depend entirely on destruction of nervous tissue and glial overgrowth, neither of which can be affected by myelotomy. Unfortunately it is not possible to distinguish clinically between the two pathological varieties of syringomyelia—the "dry" form in which gliosis predominates and surgery is useless, and the "wet" in which cavitation is the chief feature and removal of the fluid may be beneficial. In addition to draining a cavity an attempt may be made to prevent its refilling either by making the drainage opening a permanent one or by obliterating the cavity. The former may be achieved by fixing silver clips to the edges of the opening, by placing muscle tissue between them, or by suturing the lining membrane to the arachnoid on each side. In the present series the walls of the cavity, which had fallen into apposition after escape of the fluid, were painted with tincture of iodine in the hope that the resultant inflammatory reaction might lead to their permanent adhesion with obliteration of the cavity. It is to be hoped that other surgeons will record their experience so that some estimate may be formed of the proportion of cases of syringomyelia which may be expected to benefit from operation. Unfortunately it will not be possible to foretell the result in any individual case until the distinction between gliosis and cavitation can be made on clinical grounds with a greater degree of accuracy than is now possible.

### MAN-POWER OF THE DISABLED

AN injury which disables a man for the occupation he has been following does not necessarily incapacitate him for other useful work. The Minister of Labour has prepared a plan[1] for training people disabled while on war service or in civil life and for settling them again in industry. He believes that large numbers of disabled men and women could hold good jobs on their merits and not simply because of considerate treatment. For the time being preference in training may be given to war-service or air-raid victims, but the scheme will form the basis for a post-war resettlement scheme covering all persons over 16 disabled in road, industrial or factory accidents. The value of rehabilitation is not only that it fits a man to earn his living but that properly used it can restore power to damaged muscles and joints and thus reduce disability. This was proved during the last war, and remains a principle at Enham Village Settlement; it was recently illustrated by the report in our columns on 40 cases treated at the Allendale Curative Workshops.[2] The Minister of Health is favouring hospital schemes for the rehabilitation of injured people, and Mr. Ernest Bevin's plan is designed to work in with these schemes. The patient will be interviewed by a representative of the Ministry of Labour while he is still in hospital and the choice of suitable training for him will depend on his own preference, on the nature of his disablement and on the opportunity and demand in particular trades. By conferring with the physicians and surgeons in charge of the case it should be possible to arrange work within the patient's capacity, and such early contact with him should enable the ministry to plan ahead and ensure that a job is available when he is ready to take it. No doubt many patients will be able to resume their former or

1 "National Health Services." From the Secretary, 21, Claireville Grove, London, S.W.7. Pp. 46. 9d.
2. Worster-Drought, C., Wakeley, C. P. G. and Shafar, J. *Brit. J. Surg.* 1941, **29**, 56.

1. Interim scheme for the training and resettlement of disabled persons. Pp. 8. From the Ministry of Labour, St. James's Square, S.W.1.
2. *Lancet*, Nov. 1, 1941, p. 516.

another occupation without training. Information about their capacity, obtained from the hospital, will be passed to their local employment exchanges and they will be invited to seek help there if they find difficulty in getting employment.

The Ministry recognises how important it is for the man to achieve the fullest possible physical restoration both during the time he is in hospital and when he begins work, and that if he is to keep his job when peace returns he must be fitted to do not any job passably but one particular job better than most; and it must be a job which will still exist in peace-time. It may well be true, as the Minister of Labour says, that 75% of disabled people are fit to take up some kind of work again, and that they could master many of the processes now being taught at Government training centres and technical colleges. The scheme puts such training in the forefront. Since it will not be easy in such centres to give curative as well as technical training, courses are also to be provided at institutions which already have special experience of preparing the disabled for industry. In addition it is hoped that some employers will agree to provide training for disabled men. But there is some evidence that people who have qualified at Government training centres are not always being used, at present, on the work for which they have been trained. It would need much closer supervision of the factories than is now customary to ensure that the disabled employees are never given work detrimental to their condition. If a return to work produces a loss instead of an advance in power and function, it will be a disaster to the injured person instead of a benefit. All this applies with special force to patients boarded out of the Army, many of whom at present flit uneasily from unsuitable job to unsuitable job before finding one within their compass, or too often lapse into the ranks of the unemployable. Possibly, too, the official attitude to the question of reabsorption into industry has been too narrow, harping too much on surgical conditions, which though they cover most of the air-raid casualties represent only some 20% of the conditions compelling discharge of men from the Army. Medical conditions are probably responsible for almost as many incapacities among the civil population as among soldiers. Nicoll[3] has discussed the rehabilitation of the injured with reference to the coal-mining industry, and much of what he says holds for a range of disabilities stretching far beyond the results of injury.

Mr. Bevin plans that training allowances of 42*s.* a week shall be paid to men, 33*s.* to women, 17*s.* to boys and 15*s.* to girls. This wide discrimination between the rates to the sexes seems scarcely necessary, since dependants' allowances are to be paid to those in training at the rate of 7*s.* 6*d.* for a wife and 3*s.* for each child. The principle of Mr. Bevin's plan, however, is so good that we must hope to see it put speedily into force; minor defects can be put right once it is working.

## OPERATION FOR HYPERTENSION

THE experimental finding that in animals renal ischæmia will produce persistent hypertension has clinical implications which are now being explored. At a combined meeting of the sections of medicine and of therapeutics and pharmacology of the Royal Society of Medicine on Nov. 11, Prof. G. W. Pickering gave it as his opinion that experimental results will in due course explain most of the human cases of hypertension. Dr. Clifford Wilson had produced renal lesions in rats by partially occluding one of the renal arteries; pathological changes were found only in the kidney with an intact circulation and were completely absent in the clamped kidney; they consisted of fibrinoid arteriolar necrosis and endarteritis with occasional involvement of the glomeruli, and closely resembled those in sections from human cases of malignant hypertension. He suggests that the histological changes found in the kidney in the terminal stages of Bright's disease are produced by hypertension. Since the lesions in experimental animals only affect the unclamped kidney the most obvious explanation seems to be that they are caused by the hypertension, and this suggests a vicious circle: renal ischæmia leading to hypertension which in turn produces renal vascular lesions with increased renal ischæmia, and so on.

In the last year or so there have been a number of reports of hypertension associated with non-nephritic kidney disease, and in cases where the lesion was unilateral removal of the affected kidney has given encouraging results. Dr. Robert Platt, at the same meeting, described such a case in a girl of 8 who had a blood-pressure of 220/120 mm. Hg and bilateral papillœdema and retinitis. A year before, investigation for *Bacillus coli* infection had shown a functionless left kidney. The prognosis at the time of the second examination was so grave that the affected kidney was removed and proved to be small and hypoplastic. The day after operation the blood-pressure fell to 155/95 mm. Hg and five months later was only 125/70. The child has remained well and has now no swelling of the discs or retinal œdema. Similar cases of unilateral nephrectomy were summarised recently in our columns by Richardson and Smart,[1] who added 2 cases of their own to those recorded. One of these was a case of tuberculosis of the kidney and the other of hypernephroma; in both, removal of the damaged kidney caused a dramatic fall in blood-pressure maintained for several months, up to the time of publication. Barker and Walters[2] have reported successful results of operation in 5 cases of unilateral pyelonephritis. All the reported cases are readily explained by analogy with experimental results; they are generally associated with occlusion of the renal artery or vein, diminished urinary outflow, or disease of the kidney substance.

The biochemical aspects are being investigated by several groups of workers, intent on isolating the active substances produced by the damaged kidney and causing the rise of blood-pressure. Their findings up to the present were reviewed in our issue of Nov. 8 (p. 575). In the meantime it is evident that the renal function must be investigated in all cases of hypertension. Presumably many cases of hypertension with unilateral renal dysfunction might be saved by operation, provided removal of the damaged kidney was carried out before vascular changes have been produced in the contralateral kidney. An example of such a case is to be found in the report by Davson[3] of an autopsy in which one kidney showed a hydatid cyst and the other the typical histology of malignant hypertension, presumably secondary to the partial occlusion of the renal vessels of the opposite side by the growth of the cyst.

It remains to be seen what proportion of cases of hypertension are due to renal ischæmia. No certain correlation has been shown between non-nephritic kidney disease and hypertension, but Goldblatt's experiments do not suggest that the renal damage necessary to cause hypertension need be gross; in fact as a rule renal function is normal in his animals during experiments. Slight degrees of blockage in the renal arteries of man cannot necessarily be demonstrated during life by methods so far evolved, and at present the only certain way of proving that hypertension is not associated with such minor degrees of occlusion is to wait for the autopsy report. A series of such reports has been recorded by Blackman[4] who investigated the renal arteries of 50 cases of so-called essential hypertension and found the

3. Nicoll, E. A. *Brit. med. J.* April 5, 1941, p. 501.

1. Richardson, G. O. and Smart, G. A. *Lancet*, Nov. 15, 1941, p. 594.
2. Barker, N. W. and Walters, W. *J. Amer. med. Ass.* 1940, **115**, 912.
3. Davson, J. *J. Path. Bact.* 1941, **53**, 207.
4. Blackman, S. S. *Bull. Johns Hopk. Hosp.* 1939, **65**, 353.

extraordinarily high proportion of 86% with some degree of stenosis. He also found that clinical and histological evidence of vascular nephritis was present in only 56% of cases. In all 50 he found arteriosclerotic plaques in the intrarenal arteries. It is noteworthy that Goormaghtigh claims [6] to have demonstrated endocrine cells, similar to the chromophil cells of the anterior pituitary, in the walls of the renal arterioles of animals, and he states that during clamping of the renal artery these cells become hyperplastic. If his findings are confirmed pathologists may be able to demonstrate similar cells in human kidneys from cases of hypertension.

## RENAL COMPLICATIONS OF CHEMOTHERAPY

HÆMATURIA is now established as an important complication of treatment with sulphapyridine and the more recent chemotherapeutic drugs. The clinical picture produced has been described by Laird [6] in three stages. In the first stage, hæmaturia is microscopic only and pain is sometimes present; in the second, the hæmaturia is gross and usually accompanied by pain, but clears up rapidly on withdrawing the drug and giving ample fluids; and, in the third, despite such remedial measures, there is impairment of renal function which may lead to nitrogen retention, anuria and death. Treatment is straightforward, withdrawal of the drug and the pushing of fluids producing rapid improvement in cases in the first and second stages. Where it is impossible to administer abundant fluids by mouth because of vomiting or unconsciousness, 4·28% sodium sulphate with 10% glucose in normal saline should be given by the intravenous drip method. In the third stage, with anuria, ureteric catheterisation has proved a life-saving measure. Hæmaturia due to chemotherapy should be diagnosed in the earlier stages in which the simple measures are uniformly successful. It results from the deposition of crystals of the acetylated compounds in the renal tract, and Lehr and Antopol,[7] investigating the influence of urine on the crystal shape of acetylated sulphanilamide compounds, observed that the characteristic urinary crystals were not formed in highly dilute urines (sp. gr. 1014 or less). Macroscopic hæmaturia is thus most likely to develop in patients in whom the daily urinary output is allowed to fall below 1500 c.cm. It can be prevented by maintaining the daily fluid intake above 3000 c.cm., and it would be regrettable if the importance of this simple preventive measure became minimised by reports on the effects of the concurrent administration of alkali. Sunderman and Pepper [8] and Climenko and Barlow [9] have determined that acetylsulphathiazole is more soluble in alkaline than in acid urine; while Schwartz and others [10] have demonstrated a greater number and incidence of crystals of the drug in the urines of 50 pneumonia cases treated with sulphathiazole than in 50 comparable cases receiving the same drug in similar dosage but in which the concurrent use of sodium bicarbonate had rendered the urine less acid. In this investigation the urine was tested with litmus only and those giving a neutral reaction were included with those classed as alkaline; in addition, no record is given of fluid intake or the specific gravity of the urine specimens. The validity of the conclusions must be viewed with reserve until the work is repeated under more carefully controlled conditions. Furthermore, Loewenberg and his colleagues [11] have described a case of pneumonia, treated with equal amounts of sulphathiazole and sodium citrate, in which calculi of acetylsulphathiazole were found, although the urine was alkaline. Similarly with sulphapyridine there is evidence that the administration of alkali will not by itself prevent renal complications and that acetylsulphapyridine may crystallise out in alkaline urine.[12] Haviland and Bratton, in a personal communication to Sadusk and his colleagues have stated that the solubility of acetylsulphapyridine in urine remains essentially the same for a range of pH 3·3–7·4 and that its solubility at pH 7·9 is not significantly greater.

Alkalisation of the urine, then, cannot be counted on to prevent renal complications during chemotherapy, and any benefit that does result from alkalis is probably due to the diuresis they produce. But the fundamental requirement for adequate diuresis is an adequate fluid intake. We can take the patient to the water easily enough, but there is the familiar difficulty in making him drink. He must have the reason for the procession of glasses of water explained to him, and something can be gained by presenting the fluid in more attractive form, though even this is difficult now that citrous fruits are scarce. When the patient is vomiting other routes must supplement fluids by mouth. Much ingenuity will in fact be required on the part of the attendants if the necessary five pints a day are to go in, but if they are taken and retained we can be as sure as anything is in medicine that there will be no crystallisation of the drug in the renal tract.

## RADIOGRAPHY OF THE HEART

IN the examination of the heart radiography is still widely regarded as a poor second to electrocardiography. This is partly because the latter method is older and the necessary apparatus more compact. A more substantial reason however is that the information given by the electrocardiogram is usually clear-cut whereas the shape and size of the heart are subject to wide normal variation according to body-weight, shape of the thorax and movements of respiration, which must be discounted before any deductions are drawn. The value of radiology has recently been emphasised by Denstad,[13] whose work brings into prominence the pathological conditions which, hidden to clinical and electrocardiographic examination, can be revealed by radiology. Although electrocardiographic changes and enlargement often run parallel, considerable enlargement can exist with a normal e.c.g., while severe changes, such as branch block or inverted T wave, may exist with little if any enlargement. From the diagnostic point of view radiography is of great value in mitral disease where the characteristic murmurs may be indefinite. In auricular fibrillation the heart is always enlarged, and Denstad believes that fibrillation can only occur after a certain degree of dilatation has been reached. In hypertension enlargement is generally commensurate with the severity of the symptoms and is a more reliable index of the prognosis than the blood-pressure. In this as in degenerative conditions radiology is of special worth since the enlargement cannot always be determined clinically. In pericarditis radiology gives invaluable information in revealing the size of the heart itself, the degree of calcification and fixation and hence the advisability of operation. The work of Denstad and others shows that without radiology the examination of the heart cannot be regarded as complete.

5. Goormaghtigh, N. *Compt. rend. Soc. Biol.* 1939, **132**, 465; *Arch. Biol.* 1940, **51**, 293; *Amer. J. Path.* 1940, **16**, 409.
6. Laird, S. M. *Lancet*, 1941, **2**, 272.
7. Lehr, E. and Antopol, W. *Science*, 1941, **94**, 282.
8. Sunderman, F. W. and Pepper, D. S. *Amer. J. med. Sci.* 1940, **200**, 790.
9. Climenko, D. R. and Barlow, O. W. *Lancet*, 1941, **1**, 770.
10. Schwartz, L., Flippin, H. F., Reinhold, J. G. and Domm, A. H. *J. Amer. med. Ass.* 1941, **117**, 514.
11. Loewenberg, S. A., Sloane, N. G. and Chodoff, P. *Ibid*, 1940, **115**, 2069.
12. Toomey, J. A., Reickle, H. S. and Takacs, W. S. *J. Pediat.* 1940, **16**, 179. Tsao, Y. F., McCracken, M. E., Chen, Ji, Kuo, P. T. and Dale, C. L. *J. Amer. med. Ass.* 1939, **113**, 1316. Brown, W. H., Thornton, W. B. and Wilson, J. S. *Ibid*, **114**, 1605. Sadusk, J. F. jun., Waters, L. and Wilson, D. *Ibid*, **115**, 1968. Smith, E., Evelyn, K. A. and Nolan, J. F. *Canad. med. Ass. J.* 1940, **42**, 27. Wilson, C. L. and Billingsley, C. B. *J. Amer. med. Ass.* 1941, **117**, 285.
13. Denstad, T. *Acta radiol.* 1941, suppl. 40.

# Special Articles

## INJURIES AND DISEASES OF WAR

### A NATIONAL PATHOLOGICAL COLLECTION

So far no steps have been taken to replace the specimens illustrating injuries and diseases of war which was made between 1914 and 1918 and housed at the Royal College of Surgeons. These were mostly destroyed in the air-raid of May 10–11 although, as noted in the college annual report, Tonks's famous pictures of the facial injuries of the last war are intact. The college and the War Office have asked the Medical Research Council to make a new collection and a subcommittee of the War Wounds Committee has been appointed to consider how this might be done. The three fighting Services, the Ministry of Health, the Department of Health for Scotland, the Royal College of Physicians of London and the Royal College of Surgeons of England are represented on the subcommittee, and they hope that the whole profession will help in the task of collecting material. This should include specimens, pictures, photographs and radiograms illustrating lesions produced by missiles, war gases, explosion gases, secondary missiles (such as fragments of masonry or debris), crush injuries, the effects of blast in air or water, and burns from any causes; there should also be material illustrating repair, infection and the results of treatment.

#### PRELIMINARY CARE OF SPECIMENS

The value of pathological specimens when mounted depends on discriminating choice of material, the care taken in collection and the preliminary treatment. The subcommittee offers the following advice.

Only those specimens should be chosen in which the lesions can be clearly displayed.

The collector should take every care to maintain the shape and form of the specimen during fixation, when the greatest amount of shrinkage and distortion is liable to take place. A hollow viscus or any tubular structure should be suitably packed with absorbent cotton-wool soaked in formol saline, before the specimen is immersed in the fixative. Structures such as nerves, arteries, segments of bowel or slices of solid organs should be fixed in position on a suitable frame, to prevent shrinkage, bending and distortion.

Fixation should be carried out in a convenient receptable such as a bucket (only if enamelled or tinned), a basin or a jar; the volume of the receptacle should be at least twice and preferably three times that of the specimen. This ensures that the greater part of the weight of the specimen is supported by the fluid, but cotton-wool should be placed at the bottom of the receptacle to prevent flattening. Bottles with relatively narrow necks, through which specimens would need to be forced, should be avoided. The receptacle should be covered with a lid, but need not necessarily be tightly corked.

The fixative used should be 4% formol saline. Stronger solutions do not give better fixation and tend to inhibit penetration of the tissues. In the case of solid organs, with the exception of the brain, the fixative never penetrates more than about ¼ in. For this reason all dissection and trimming should be carried out before fixation is completed.

The fixative is made up of: sodium chloride 9 g.; commercial formalin (40% formaldehyde) 100 c.cm.; water 1000 c.cm. Formalin solutions tend to become acid by oxidation to formic acid, and it is important that any acid formed should be neutralised. This can be done by adding a small quantity of carbonate of magnesia (mag. carb. pond.), chalk or marble chips to the stock solution, which should be stirred occasionally. The clear neutralised fluid for fixation can then be decanted as required.

The specimen should remain in the fixative until it is sufficiently hardened for safe dispatch by post to the receiving depot, where fixation will be completed if necessary. The time required varies considerably with the nature of the specimen. Small delicate specimens will be adequately fixed in a few hours, whereas larger, fatty specimens may require a week for fixation. Since glycerin and other mounting fluids are now almost unobtainable, no large-scale attempt will be made at present to restore the colour of specimens. The specimens will be stored in separate containers to prevent crushing and distortion, and they will be mounted when supplies of mounting fluids are available.

For dispatch by post, a specimen should be taken out of the fixative, drained of excess fluid, wrapped in lint moistened in fixative, and covered with jaconet. The parcel should then be packed in dry wood wool or sawdust, in a suitable box. The dry packing should be sufficient to prevent leakage during transit, and the box should be clearly labelled "Pathological Specimen." A precise history should be sent with each specimen, giving the cause of the injury, treatment and clinical progress, and emphasising any pathological point that the collector regarded as important. The name and age of the casualty, the hospital concerned, and the name of the collector should be stated. The history may be sent by separate post, or in the box with the specimen, provided that the papers are protected from damage by moisture. An acknowledgment, with comments on the condition of the specimen on arrival, will be sent to the collector.

Specimens are to be sent in the first place to one of two receiving depots where they can be temporarily classified and stored. For Scotland and the north the depot is the pathological department of the University of Leeds, and specimens should be addressed to Prof. M. J. Stewart. The depot for the south is at Hill End Hospital, St. Albans, Herts, and specimens should be addressed to Prof. Geoffrey Hadfield.

## MEDICAL WAR RELIEF FUND

SINCE this fund was set up just over a year ago over £34,000 has been contributed by the medical profession at home and overseas to provide immediate help for British doctors and their families to whom the war has brought financial hardship. The need is sometimes temporary but it is almost always urgent; and within a few weeks of the fund's beginning the distribution committee had made its first awards, and during its first year 44 applicants have been helped with a total call on the fund of nearly £5000. They include the dependants of 5 doctors killed on active service; 16 doctors whose homes or consulting-rooms have been damaged by bombing; 7 who have lost their practices as a result of evacuation; 8 whose incomes dropped when they joined the services or who needed help to set up in practice again after resigning their commissions because of ill health. An award was also made to the wife of a doctor who has remained in one of the Channel Islands after the German occupation. The following three cases illustrate the scope of the work:

Dr. G., a senior general practitioner, lost his life in a raid in which his house was completely destroyed. His only child was killed at the same time. The widow lost her clothing and other possessions, and although the doctor's estate would eventually furnish her with a modest income, she was temporarily without means. She was awarded a suitable sum as a gift to provide for her immediate needs.

Dr. M., a specialist serving in the R.A.M.C., was killed on active service, leaving a widow and child. Mrs. M. has been awarded a gift (to be administered by the Royal Medical Benevolent Fund) which will supplement her small income during the child's remaining years at school. As Dr. M.'s elderly mother had been partially dependent on him a similar arrangement has been made in her case; and Mrs. M. senior has been introduced to two other benevolent societies, one of which has awarded her a small grant while the other has given more permanent assistance in the form of a small pension.

Dr. K. is an elderly consultant. His consulting-rooms were bombed and destroyed with the furniture, instruments and books which they contained. The income from his practice had diminished owing to the war and, although he had no debts of any magnitude, neither had he the means to acquire new premises and equipment while awaiting the payment of war-damage compensation. He was awarded a substantial sum for this purpose—the greater part as a loan and the remainder as a gift.

These cases show grants to widows and dependants which have been made as gifts, but where the applicant was a doctor whose troubles seemed to be temporary part of the help was given as a loan and some of these are already being repaid. The gifts amounted to £4795 and the loans to £3040. The distribution subcommittee of the fund has worked in close coöperation with the Royal Medical Benevolent Fund and acknowledges its debt to the accumulated wisdom and experience of that body. Not only has the R.M.B.F. provided applicants with persuasive introductions to other funds which have granted supplementary awards, but it has undertaken the administration of long-term educational grants, an arrangement which will assure widows with young children of continued counsel and help when the work of the war fund is happily accomplished.

The generosity of the B.M.A. and R.M.B.F. has made it possible to keep the administrative costs of the fund for the year down to £150, or less than 0·5% of the amount

contributed. Economical administration and discerning distribution are necessary, for the greater part of the fund's work is believed to lie ahead. Contributions may still be sent to the hon. secretary at B.M.A. House, Tavistock Square, London, W.C.1.

## OUTPUT AND THE WORKER

### "APPLY EXISTING KNOWLEDGE"

THE 21st report of the Select Committee on National Expenditure [1] dealt with labour problems and war output, and the Government has now published as the 25th report [2] of the committee a detailed commentary on these recommendations. The replies are divided into broad categories such as hours of work, wages, management, discipline, industrial relations, transport, food, lighting in factories, and incentives to output. In the main the Government finds itself in agreement with the views of the committee but differs on some details. For instance, it is implied that the committee did not have a clear idea of the functions of the Industrial Health Research Board when it recommended that the board should work in the closest coöperation with, and advise the production departments. The responsibility of advising these departments on factory conditions and the health of the workers belongs to the Ministry of Labour—presumably through its Factory Department lately transferred from the Home Office—and the function of the board is to investigate general scientific problems. Another recommendation was that the board should carry out investigations to determine the best length of the working week for a wide range of different kinds of work and for men, women, and juveniles; but the board has been doing this kind of work for many years—its first emergency report [3] was a summary of its findings since the last war—and as it has indicated that weekly hours of work should not exceed 60 for men and 55 for women, it appears more useful to apply existing knowledge than to undertake further investigations which would be unlikely to produce different results. It is proposed, however, to carry out further inquiries into the conditions of some sections of industry and of particular kinds of work and to ask for the board's help.

The recommendation that workpeople should have one day's rest in seven has, in the Government's view, been confused with the question of Sunday labour. The committee is reminded that they said in their 17th report that the general atmosphere of Sunday is not conducive to the maximal effort, and with the object of maintaining production at its highest level most of the departments concerned agree that Sunday work should be restricted to essential maintenance or repair work and emergencies. Some aircraft firms have reported that Sunday work has been given up with beneficial results on output. Some workers have resisted the abolition of Sunday work because they receive double pay for that day, and the Government cannot accept the committee's recommendation that the loss of the extra payment for Sundays should be taken into account when fixing wage rates for week-days. It seems that 5½ or 6 days a week on production work is the best system which can be arranged and that rota systems are not easy to run because of the additional labour force required and inherent difficulties in organisation and supervision. The policy of the Government is, however, that factories should be employed for as much of the 24 hours as possible, and an increasing number are working round the clock.

In addition to the committee's recommendations employers have been urged to adapt women's working hours to allow them reasonable time for shopping and in some factories this has been done. Discussions have been held with retail trade organisations and with the Ministry of Food and shopkeepers are to be asked to keep their premises open for longer hours on one more day a week and to adjust the shop lunch-hour to suit the industrial workers, who may also leave written orders for goods to be collected after closing time.

The Government fully endorses the policy that managements should, where possible, take workpeople into their confidence and both groups are encouraged to come together for the exchange of information and experience. We said recently [4] that if workers are treated like children they will act like them and it is encouraging to see that the lesson is being slowly and painfully learnt. It is agreed that men should be appointed to positions of authority in industry, particularly as charge-hands and foremen, for their qualities of leadership and organising ability as well as for their technical skill. Publicity has been given to the established training courses for personnel managers, welfare supervisors, and foremen, and also to the work of the conciliation officers of the Ministry of Labour whose main function is to intervene when disputes arise between unorganised sections of industry and employers who do not recognise trade unions. It is emphasised that any publicity which created an impression that the services of the conciliation officers were immediately available to settle disputes by direct intervention would tend to undermine the constitutional authority of employers' organisations and trade unions.

In reply to a recommendation that a persistent offender who refuses to obey a direction under the Essential Work Order should be dereserved, the Government states that it has always been made clear that men are kept out of the forces for the purpose of working assiduously and those not doing so will not be allowed to remain reserved. But the specific proposal that military enlistment should be regarded as a penalty for industrial offences is open to objection and it would not meet with the support of the workers, nor, it might be added, of the armed forces themselves.

Transport difficulties and the measures needed to overcome them are discussed at length. The arrangements for supplying food to the workers are described and the Government cannot accept the recommendation that the Factories (Canteens) Order, 1940, should be applied to all factories doing work for the Crown, and not only those employing more than 250 people. For the smaller factories the policy is to establish British Restaurants nearby and the workers can either go to them or have meals sent to the factories. The committee pointed out in their report that speeches congratulating workpeople on their efforts make for complacency, but the Government says there is no need to stimulate them to greater output on the basis that their best efforts have been feeble and unsatisfactory. It probably should have been stated more definitely that if a worker is praised he will respond and will not become slack because he has been made to feel that he has done his best. There are varying types of complacency or states of euphoria. Report answers report on the whole satisfactorily and shows that constructive thought is being given to constructive criticism.

1. *Lancet*, 1941, **2**, 341.
2. 25th report from the Select Committee on National Expenditure. London: H.M. Stationery Office. Cmd. 124. 6*d*.
3. See *Lancet*, 1940, **1**, 699.

## Infectious Disease in England and Wales

### WEEK ENDED NOV. 8

*Notifications.*—The following cases of infectious disease were notified during the week: smallpox, 0; scarlet fever, 1366; whooping-cough, 2029; diphtheria, 1069; paratyphoid, 31; typhoid, 12; measles (excluding rubella), 747; pneumonia (primary or influenzal), 731; puerperal pyrexia, 108; cerebrospinal fever, 113; poliomyelitis, 33; polio-encephalitis, 4; encephalitis lethargica, 3; dysentery, 148; ophthalmia neonatorum, 84. No case of cholera, plague or typhus fever was notified during the week.

The number of civilian and service sick in the Infectious Hospitals of the London County Council on Nov. 5 was 1315, including scarlet fever, 166; diphtheria, 298; measles, 23; whooping-cough, 505; enteritis, 32; chicken-pox, 28; erysipelas, 22; mumps, 5; poliomyelitis, 6; dysentery, 23; cerebrospinal fever, 22; puerperal sepsis, 8; enteric fevers, 45; german measles, 1; other diseases (non-infectious), 62; not yet diagnosed 69.

*Deaths.*—In 126 great towns there were 1 (0) deaths from enteric fevers, 1 (0) from scarlet fever, 1 (0) from measles, 2 (0) from whooping-cough, 24 (6) from diphtheria, 41 (2) from diarrhœa and enteritis under 2 years, and 20 (0) from influenza. The figures in parentheses are those for London itself.

Bristol reported 1 death from an enteric fever. There were 3 fatal cases of diphtheria at Liverpool.

The number of stillbirths notified during the week was 164 (corresponding to a rate of 32 per thousand total births), including 13 in London.

4. *Lancet*, 1941, **2**, 566.

# In England Now

*A Running Commentary by Peripatetic Correspondents*

IF the G.P. of the future is not to be a martyr to writer's cramp, ambidexterity must be forthwith introduced into the curriculum. Certificate-writing has a great future. At present it is only in its infancy and probably does not occupy more than a quarter of the doctor's working day. I don't think that I am ever called on to sign more than 35 different kinds of certificate. Let's have them all in during one surgery hour (as well we may) and tot them up. First, then, we have A, a farmhand with an infected toe. That's easy. Obviously he can't work till his toe is better, so I give him a weekly panel certificate. In totters old B with paralysis agitans. He gets a pink certificate, so that I don't have to write another one for him for a whole month. Ah, wait a bit—he belongs to two private clubs which pay him a few shillings and he might as well have them, so I sign them for him. Total so far, 3. Mrs. C brings in her little boy with a cough. He is, she tells me, on the natural deposit and produces the appropriate form—only diagnosis and initials to be written on that one. Her husband has also looked in because he has broken his plate, so he gets a certificate stating that he requires dental treatment. In comes Miss D; she gets headaches, worse after sewing or reading, and she thinks, quite rightly, that she needs glasses. I give her an ophthalmic certificate and call for the next patient. It is Mr. E, big, fat and elderly, to say that his truss is almost wear'd out and he needs a new one. I give him a certificate for a surgical appliance and mop my brow. Total to date, 7. Mrs. F. has sent up her little girl with a certificate claiming maternity benefit. The nurse could have signed this, but Mrs. F forgot to ask her when she was attending, so perhaps the doctor will oblige. He does. Oh, and Mrs. F wants an extra milk certificate for nursing mothers; and Auntie, who is expecting, wants one too—10 up. The wife of a sailor wants a form signed so that she can draw her separation allowance; she is followed by the wife of a soldier and the wife of an airman in similar circumstances. Total, 13. Old Mrs. G and her widowed daughter, Mrs. H, come in together. Mrs. G wants her O.A.P. paper signed and Mrs. H one for the widows' pension. A J.P., lawyer, minister of religion or other responsible person could sign these, but the doctor is unfortunately so much more accessible than other responsible persons. Hello, here comes young I, the telegraph boy, with an almost invisible dog-bite. There is a regular questionnaire to fill in about this, but it is done at last and I makes way for his father, a postman, with lumbago. He can't work with lumbago, poor chap, so I give him a post-office certificate. 17. Mrs. J's husband is a diabetic so needs a certificate for the food office; and could she have a certificate so that she may get glucose for the baby? You know how he needs glucose, doctor. And you said little Charlie wasn't to go back to school till his throat was quite better—well, the school attendance officer keeps badgering her, so could she have a note to show him No. I dig in my toes. If the school attendance officer won't take her word for it that little Charlie is under the doctor, let him come and see me. That settles the school attendance officer and gets me out of writing one more certificate. Mr. K is still far from right in his stomach in spite of the operation which I said would cure it. I didn't, but agree that he should have extra milk and write a certificate accordingly—20 up. Miss L is a nice, bright girl and won't keep me a minute. Just sign this to say that she is fit for work in the NAAFI. I examine her, answer the questions and sign. Mr. M is going to work in the dockyard and has a special form for me to fill in and sign—I examine him and do so. At this point the relieving officer creates a diversion by looking in to say that old Miss N who was always a little odd, has identified herself with Hitler, and, in a state of nature, is haranguing the delighted multitude from an upstairs window. I slip out and certify her. Back again, I find Mr. O in great distress. He lost both legs in the last war, has mitral stenosis and has been called up. The man at the labour exchange agrees that Mr. O is probably unfit for national service but must just have a line to that effect from his doctor. Mr. P really does not take long. He is recovering as quickly as he can from a number of bomb wounds and blast effects, but has to have a weekly certificate of unfitness to work. It's all a lot of red tape, he says, but I rebuke such levity. Mrs. Q says that my partner has ordered her daughter to go under the X rays in hospital and she has brought the hospital-aid form for me to sign. Mrs. R's old father has passed away at last. We agree that it's a merciful release for all three of us. Even in death he is a nuisance, requiring not only a death-certificate but a cremation-certificate as well. 28. Only two more patients I see. Here's Mr. S who has been pulling turnips and got a tenosynovitis; that means an industrial diseases certificate. And Mr. T has been knocked over by a car. He isn't badly hurt, but I must fill in a road-accident form. Apart from sending off a throat swab, a sputum, a blood for W.R., a specimen of urine and a request for an X-ray report, all of which require certificates, that seems to be all. Yes, I make it 35 kinds. When I get home, if ever, I can fill in the antenatal examination, emergency midwifery and vaccination forms and write letters to the county council recommending children for T's and A's.

* * *

It is not altogether surprising that from time to time the less sensational elements of the lay press look with a tinge of suspicion at successive blasts of semi-official eulogy in praise of this or that source of vitamins. It may sometimes appear that the changes are rung a trifle freely on the virtues of many things as they happen to hang heavily on the official hands—sometimes carrots, sometimes rose-hips. We have recently succumbed to the rose-hip propaganda, and have organised expeditions of our nursing staff into the country lanes in search of berries, "vivid red and slightly soft" to quote the official instructions. There is no dearth of volunteers for these outings, despite the fact that the collection of rose hips is known to be prickly, devastating in its effects on stockings and sometimes rather dirty. By way of compensation, it involves a not-too-smooth ride a few miles into the countryside, a picnic forenoon and a departure from everyday routine. Raiment of ancient vintage is pulled from obscurity, and the party sets out in a gay spirit of adventure, though scarcely, perhaps, a very fashionable gathering. The instructions for picking are explicit enough. The fruit is not to be bruised or in any way damaged, and the berries brought back as soon as possible after picking in suitable containers—"baskets, not tins."

Back at the hospital the work of extraction begins. The hips are placed in a pan, covered with water and subsequently mashed with a wooden spoon, and the mass squeezed through a jelly bag to obtain the juice, care being taken to filter out the sharp, stiff hairs on account of their reputed capacity to produce gastric irritation. Our instructions were that the fruit should be boiled for about a quarter of an hour until tender, which seemed a little odd in view of the known properties of vitamin C; and we found when we tested the vitamin content of brew prepared in this way that the prescribed boiling for a quarter of an hour was highly prejudicial to vitamin-C content, reducing it to about a third of what it had been at the boiling point. On the other hand, nothing short of boiling succeeded in extracting any considerable quantity of vitamin from the fruit, so that we were driven to compromise by slow raising to the boiling point, with discontinuance of heating as soon as that was reached. We were able in this way to obtain an extract of fairly stable vitamin content, though it fell considerably short of the impressive figures issued with the official instructions. From the juice we prepared a syrup by the simple addition of sugar, and hope piously that the resultant product will keep with us for a period of three months. We estimate that it will be necessary to take 3 oz. of the syrup daily to produce any appreciable effect.

The next problem was to determine how best it could be used. In our early enthusiasm we had hoped to carry out something in the nature of a controlled experiment that would enable us to record any improvement in health among the rose-hip takers, but we soon found that an experiment of this sort on any worth-while scale was out of the question, and we had to content ourselves with the selection of a score of nurses who seemed to experience habitually more than their share of the ills of this world. These unhappy people were singled out as experimental

animals and elaborate precautions taken to ensure that they duly consumed the syrup. Whether it will do them any good we are not yet in a position to say; it can scarcely do them much harm, unless some of the "sharp, stiff hairs" have eluded us. But, almost irrespective of the outcome, we have come to the conclusion that the game is scarcely worth the candle and that the chief virtue of our essay in rose-hip extraction lies in its significance as a gesture of benevolent interest. We have had much the same feeling about the outcome of our attempts to grow oats and potatoes; but in war-time we do, with the official blessing, many curious things. Rose-hip jelly as a jelly may be quite good, even appetising, but the treatment of rose-hips on the domestic hearth as a source of vitamin C seems to be rather an overrated amusement.

* * *

After several false starts traceable to the water-pipes or to the singing of high-spirited colleagues and military policemen Wailing Willie really got going the other night, warning us of the unpleasant proximity of Hitler's young friends. Our siren is no ordinary one. Its voice is well and truly broken and in full cry resembles a byre at milking time or the ear, nose and throat ward on tonsil morning. Like the heating system its efficiency depends on the steam pressure and varies accordingly. When the fires are banked up well and there is no other claim on its motive power its roaring is echoed and re-echoed from the hills like the wail of the last of the banshees, but on one famous night when the fireman had fallen asleep and let the furnace go down all that Willie could do was to give an apologetic gurgle such as follows removing the stopper from a bottle of flat ginger beer. As ill luck would have it that very night the all-clear came within five minutes and the raiders-past signal lacked its usual triumphant ring.

The garb in which the various members of the staff parade on such occasions is to me a never-ending source of interest and amusement. I myself am sufficiently hidebound in the fetters of convention to regard the absence of a collar and tie as the last infirmity of noble mind and dress accordingly. Such opinions are not held by my colleagues. The Physician, as all good physicians should, upholds similar ideals to my own but the very fountain head of orders has been known to appear wearing a lounge suit on top of his pyjamas; in extenuation, however, it must be said that the occasion in question was the third of three successive nights. Some version of engineers' dungarees which our female friends assure us is termed a shelter-suit seems to be favoured by the junior members of the medical staff of that sex and I have found it in my heart to envy them when searching half asleep for a lost collar-stud at two in the morning. The nursing staff, however, are allowed no such easily put on garment, but they are probably well used to dressing in the earlier stages of coma at 6.30 A.M. and little deserving of our sympathy. They at least can put a cap over their curlers when rudely awakened, but the mere male who appears with untidy hair is frowned on by all alike.

The wail of Willie is the signal for action stations for the fire-watching parties, who proceed armed with stirrup pump and sand to their appropriate places. The selection of one's appropriate locus is not as simple as it sounds since our firemaster, one Sir Thomas Tucker, erstwhile leading light of the brigade in a provincial town, has an engaging habit of changing this about once a week without notice. He has even been known to go off on holiday and take his beloved stirrup pumps with him for a change of air. It is true he left us the hoses but according to his own teaching these are an invention of the devil only to be used by experts (for which read "himself"). Despite these interesting diversions it is always with a grievance that I leave my warm and comfortable bed to watch for incendiaries which never fall or to shelter from high explosive dropped fifty miles away.

---

MESSRS. T. J. SMITH and NEPHEW have issued a second edition of their booklet "The Preparation of Plaster Casts," which includes patterns and directions for a spinal jacket in addition to the six plasters described in the first edition. The booklet can be obtained free of charge, and a set of master patterns made of stiff paper is supplied with the first order for wide "Cellona" material.

# Parliament

## ON THE FLOOR OF THE HOUSE

MEDICUS M.P.

ON Nov. 11 Parliament was prorogued. It was, to quote Hansard, "End of the Sixth Session (opened 21st November 1940) of the Thirty-Seventh Parliament of the United Kingdom of Great Britain and Northern Ireland in the Fifth Year of the Reign of His Majesty King George the Sixth." But it was only a winding up on Nov. 11 in order to open a new session on Nov. 12, so the Speaker suggested that the custom of all members filing past him, shaking his hand and bidding him farewell, should be dropped. "On this occasion I bid you farewell from this place and hope soon to meet again."

The King's speech on the prorogation of Parliament referred to the Atlantic Charter as "a beacon in history radiating resolution, justice and unselfish purpose" and to conferences with the prime ministers of Canada, Australia, New Zealand and South Africa. The King's speech on the opening of the new session on Nov. 12 referred to consideration of "the urgent problems which will face them when the nations now enduring the tyranny of the oppressor have regained their freedom" and further welcomed the restoration of the Emperor of Ethiopia to his throne as the first country to be liberated and re-established.

The content of these two statements of policy do not satisfy the House of Commons. There is a widespread feeling that changes in policy are required—with regard to production for war purposes, with regard to the direction of our military efforts, with regard to interference with individual liberty centring round the use of the powers of Defence Regulation 18B, with regard to the allowances of wives, children and other dependants of men in the forces. All members support the war effort of the Government but many think it should be intensified and that it should take cognisance of those larger issues of political and economic change that loom in men's minds in prefigurement of the future. Sir Richard Acland, the wealthy landowner who is serving in the ranks in an Army Unit, emphasised these larger issues. Contrasting this war and the last he said, "In this war there is a positive and passionate longing on the part of the overwhelming majority of the people not to go back to the miserable world which they knew in 1939. We want to move on to a new way of living where the motive of service will transcend the motive of individual gain." Acland referred to a meeting he had had with a very "tough set of successful business men" who all wanted "a Britain without property owners" and ended by what was in effect an appeal to Winston Churchill to take the lead in a complete renewal of Great Britain's economic and social structure.

* * *

Major E. E. Gates, in a well-delivered maiden speech dealing with the anomaly of the difference in pay between the services and industrial workers, ended, "Unless the Prime Minister devotes himself closely and immediately to our pressing domestic problems with the same brilliancy that he has so far devoted to the grand strategy the war may be lost in these islands."

Mr. Austin Hopkinson said this war was "really Armageddon" and that it would from the biological point of view decide the future progress of the human race. He regarded the present war as the climax of human history and as embodying the conflict of principles which had been perceived clearly for 3000 years. "In one country after another, in Northern India, in Greece and finally in Palestine one man after another has arisen and said that the whole human race is going to ruin—and that until men really believe, and act upon the belief, that it is better to give than to receive, there is no hope whatsoever for the future of humanity."

* * *

Mr. D. N. Pritt, K.C., criticised the continued presence in the Government of men who were "extremely lukewarm" towards our alliance with the U.S.S.R. Mr. Shinwell reaffirmed the essential unity of the nation and our determination to effect the speedy destruction of Hitlerism but made a powerful and sustained criticism

of Government policy urging better organisation and more speed in work. "The essence of victory lies in speed, in audacity, in taking risks, and in dauntless courage. Unless the Government can supply these virtues, they will, in the opinion of the country, have outstayed their welcome." Mr. Lloyd George went over to Shinwell after the speech and congratulated him—Conservative, Liberal and Labour M.P.s did so too. Mr. A. V. Alexander's reply to the debate in which he dealt largely with Shinwell was on lines of personal attack and produced a bad impression on the House and he passed over the big questions raised by other members without remark.

* * *

The Prime Minister had stated earlier in the day that a full debate on the address might, if desired, extend over 2 or 3 weeks. Parliament is awake and a succession of debates on big issues of policy is certain. Mr. Churchill does not now propose to make any changes in membership of the Government.

## Obituary

### HUGH MORELAND McCREA

O.B.E., M.D. R.U.I.

BY the death of Hugh Moreland McCrea a very remarkable man is lost to our profession. The qualities in the aggregate required to make a great clinical physician are much more rare than those needed to make a great surgeon, for the problems presented to the latter are solvable chiefly by touch, sight and personal dexterity, whereas those with which the physician has to cope require, not only the piecing together in order of importance of a number of data obtained from various sources, but the correct deduction from the whole assemblage.

*Vandyk.*

The power of doing this varies with individuals, but from time to time men appear who, possessing a faculty for retrieving and marshalling in surprising context impressions latent in subconsciousness, have it in remarkable degree. The term *flair* is commonly used to describe this faculty and McCrea was one of those gifted persons. To the gift was added an insatiable zest for professional knowledge which was continually added to by acute observation and voluminous reading. The result was a many-sided physician without one weak facet, so that whatever the nature of the case he brought to it the ability of an expert on that particular malady. He was at first in general practice, surely the best of all preliminary schools for a career of pure medicine; but, like certain other great physicians who began that way, the call to consulting work at last assumed imperative proportions. His outstanding professional qualities became so widely recognised that he may justly be termed the consultant's physician, so many of them were numbered amongst his patients.

His energy and kindness matched his abilities, for he threw his whole heart into every case, great or small, to which he was called and a multitude is in his debt. His passing enhances a regret, often felt before, that he was never on the staff of a teaching hospital where the high ideals and deep mine of clinical lore of which he stood possessed could have been passed on to the younger men coming after him. Amongst those of us who knew him he will always be remembered as a beloved physician and an unfailing help in time of trouble.

V. B.

McCrea was born in 1877 at Belfast, where his father was a medical man of considerable distinction and his maternal grandfather was Dr. R. Dill, professor of midwifery at Queen's College. He was at school at the Royal Academical Institution before entering Queen's University on a science scholarship. He took the Malcolm exhibition and the Coulter clinical scholarship, qualified M.B. in 1901 and for two years held resident appointments at the Royal Victoria Hospital. In 1903 he settled in general practice at Wargrave, whence he moved to London four years later. He combined a rare acumen with a profound knowledge of modern tendencies and of the various branches of medicine. He was specially familiar with the many problems which ophthalmology presents to the practitioner of medicine and the ophthalmoscope revealed much to him which would have been hidden to many. He was for long on the outpatient staff of the Paddington Green Children's Hospital and during the last war acted as senior physician to the City of London Military Hospital. He became chairman of the Final Medical Appeal Board and he organised the emergency medical corps under the auspices of the Royal Society of Medicine. For these services he was made O.B.E.

The idea of forming a vast private hospital where private patients would have at their service the same advantages as those enjoyed by patients in the voluntary hospitals early took root in his mind and soon after the war finished he set about, with indomitable energy, to realise his dream. The result was the London Clinic of which he was the originator and principal promoter. When in the years to come such institutions have grown up in all the great centres of population, working either independently or in association with the voluntary hospitals, it should be remembered that McCrea pioneered the way.

For some time his health had given rise to anxiety but the end came on Nov. 8 with unexpected suddenness. He married Kate Rose, daughter of Charles Hannen of the Chinese Customs, and leaves his widow with two daughters.

### MILLICE CULPIN

L.R.C.P.E.

Dr. Millice Culpin, who died at Brisbane on Sept. 1 at the age of 95, was Queensland's oldest doctor. He was born in this country and began his schooldays at Alleynes Grammar School, Stevenage, shortly before the outbreak of the Crimean war. He qualified L.S.A. from the London Hospital in 1877 and took the Scottish conjoint qualification five years later. He set up in practice in Brisbane over sixty years ago and soon all his interests were centred in his new home; except for one holiday many years ago he never returned to England. He represented Brisbane in the federal parliament from 1903 to 1906, but public life was to him a duty, faithfully performed, and his real interests were his work, his books and chess. He was also a member of the Rationalist Society of Queensland. Dr. Culpin leaves three daughters, and his two surviving sons are both members of the medical profession—Prof. Millais Culpin of London and Mr. Ernest Culpin of Brisbane.

TRAINING THE LUFTWAFFE DOCTOR.—The medical officer of the Luftwaffe seems to be a true son of the winged Hermes, for he is trained to be both doctor and flier (*Dtsch. med. Wschr.* Sept. 12, 1941, p. 1018). After taking his Abitur—which is the equivalent of our matric—the candidate does six months' military training before joining the medical academy of the Luftwaffe, which is at present housed in a suburb of Berlin. Here he is taught the principles of aviation and at the same time begins his medical studies. But his military training also continues, and is considered an important part of his curriculum, for in spite of the Geneva convention the German medical officer "often has purely military tasks of leadership to fulfil." So that he may lead medical flying units and cope with the problems of aviation medicine and flying in high altitudes the student must himself learn to fly gliders and planes, and he must be able to manage not only the larger types of aircraft used for the transport of casualties but also the smaller makes such as the "Storch" and "Weihe," for they have the advantage of being able to land in a confined space. He is also taught to use a parachute, for if he joins a company of paratroops he must be able to jump with his men. Institutes for research in aviation medicine have been set up in Hamburg, Freiburg-i-Br., Jüterbog and Berlin.

# Letters to the Editor

## WORKING HOURS

SIR,—In September, 1915, Mr. Lloyd George, then minister of munitions, appointed a Health of Munition Workers Committee, "to consider and advise on the question of industrial fatigue, hours of labour and other matters affecting the physical health and physical efficiency of workers in Munition factories and workshops." The committee recognised that if men are asked to work for fifteen hours a day for weeks and months on end, as was the case in 1916, one of two results must follow: either the health of the workers will break down or they will not work at full pressure. In either case output must suffer. The committee made the provisional recommendation that hours of work for men should not exceed 65–67 per week; for women and girls 60, with no night work for girls under eighteen; and for boys under sixteen, 60 hours with no night work. In 1917 the committee stated that they were convinced that the maximum limits of weekly employment provisionally suggested were too high except for quite short periods and that the time was then ripe for a further reduction in the hours of work. They were satisfied that reduction could be made with benefit to health and without injury to output.

It is some 120 years since Robert Owen ran his New Lanark Mills for only 10½ hours a day instead of the usual 15–16 and found that output did not sensibly fall below its previous level, while there was marked improvement in the cheerfulness of the operatives and in their vigour. The events of the last war demonstrated beyond question that there was a point beyond which it was folly to extend hours of employment and that that point was much lower than had been accepted previously. Subsequent work carried out under the auspices of the Industrial Health Research Board has all pointed in the same direction. Vernon in his book "The Health and Efficiency of Munition Workers" suggested that the optimum working hours for women are between 48–54 per week, and girls under 18 should not be required to work more than 48 hours per week. It is only after two years of war that these well-established principles have received some measure of official sanction. The Government comment on a recommendation in the 25th report of the Select Committee on National Expenditure, issued recently, recognised that investigations by the Industrial Health Research Board have established that, over an extended period, weekly work hours should not exceed 60 for men and 55 for women, and the Government is satisfied that it is more useful to restrict weekly hours now within the limits mentioned than to make further investigations. It is officially agreed that, to maintain maximum production, Sunday work should be abolished in industry, except to meet the most compelling emergency and except in those plants where workers have a break of at least 24 hours per week under a rota or relief system.

It is a matter for profound regret that it has taken so long to relearn such an essential lesson of the last war, and it is to be hoped that never again will there be a temptation to succumb to some of the follies in this matter of working hours that have been perpetrated during the last two years.

DUNS SCOTUS.

## PNEUMOCOCCAL MENINGITIS

SIR,—So many reports of the recovery of isolated cases of "pneumococcal meningitis" have now been made that one would gain an impression that the outlook had very materially altered since sulphapyridine was introduced. I am sure there must be many clinicians like myself who feel that this scarcely reflects the true state of affairs, and who are therefore grateful to Dr. Cooke for his significant paper in THE LANCET of Nov. 1.

There are two observations I would like to make on your annotation of Nov. 8. When assessing the results of treatment is it satisfactory to lump all cases under the generic term of pneumococcal meningitis? My own experience leads me to subdivide those cases into three groups. First the *septicæmic case* where meningitis is a late, often terminal, complication of a pneumococcal infection distant from the meninges; second, the *invasive case* where meningitis is a result of local spread from a focus of infection close to the meninges; and third, the *traumatic case* where the infection is caused by the passage of organisms from the nose or throat through a breach of bone (this last including the postoperative case). Such a subdivision has, I think, considerable importance in relation to chemotherapy. Septicæmic cases occur even during the course of sulphonamide therapy, and presumably this indicates that either the organism is insusceptible to the drug or the patient is unable to utilise it; the fatality-rate in this group is still high. In the invasive case sulphonamide therapy may, for the time, discourage further invasion, but will almost certainly not eradicate the primary focus, for which surgery will still be required if recurrence of the meningitis is to be prevented. In the traumatic case, however, sulphonamides may be expected to show optimal results, for the organism is here probably of low virulence and its invasiveness may therefore be promptly checked. The clinician's assessment of the value of chemotherapy will thus depend on the kind of case he is called on to treat.

My second point is to ask for the evidence which supports the statement that type III is the "most common single type in this infection." I cannot recollect having seen a single type III infection of the meninges. My earlier records are unfortunately not readily available, but I have seen twelve cases since 1938 in which the types were: II (4), V (1), VI (2), VII (1), XIII (1), XXIII (2) and one where the pneumococcus did not agglutinate with any of Cooper's 32 types. None of these cases recovered despite the administration of sulphapyridine. Only three of them did not belong to the septicæmic group. The type VI was caused by an antral infection, while the type XIII was secondary to a mastoiditis. There was no apparent primary focus in the case from which the untypable strain was obtained. (It is at least arguable that the comparatively rare primary pneumococcal meningitis should be included in the septicæmic group.) I can readily understand that type III, which is so often present normally in the nose or throat, might be most frequently encountered in the traumatic group: but I can see no reason for supposing a high incidence of this type in the septicæmic or invasive group. In these groups one would expect the type incidence to correspond to that peculiar to the district from which the cases were drawn.

Knightswood Hospital, Anniesland. THOMAS ANDERSON.

## WHEN TO TIE THE CORD

SIR,—I was interested in your leading article of Nov. 8 on when to tie the cord. It always seems to be taken for granted that the baby will gain extra blood if delay is made before applying the ligature until pulsation in the cord has ceased. I suggest that this is contrary to the truth and that the baby is liable to lose blood by this delay. In any case I think the following argument is worth consideration. From the point of view of the welfare of the babies the matter is of importance. It is obvious that the only force propelling the fœtal blood-stream, and hence that part of it going to and coming from the placenta, is the fœtal heart beat. This force is of only moderate power and yet it is the only force available for the return of blood from the placenta to the fœtus. This is a great task for a comparatively weak organ to fulfil. Intermittent uterine contractions during the third stage obviously can be of little or no account in this process. Consider the work that the heart must do and the conditions prevailing. The placenta is an inert body and is, in the third stage, largely unsupported. Therefore, before any blood returns to the fœtus the placenta must fill up and form what is equivalent to a heavy lake of blood. The fœtal heart must take on the strain of overcoming the resistance of this inert and heavy lake in order to force any blood at all back to the fœtus through the umbilical vein. It is practically certain that the task is too great and that far more blood remains in the placenta than ever returns to the fœtus. Thus the fœtus will lose more and more blood the longer the flow continues to go into the placenta. But the fœtus may lose blood in another way as well. There may be a certain amount of separation of the placenta and there may thus be direct fœtal blood loss through the separated placental surface. It is true that anatomically the placenta separates from the uterus

through maternal tissue and so it may be said that the placental surface is sealed in such a way as to prevent loss of blood through the separated placental surface. But where such a very thin covering is involved there is bound to be much tearing and it is likely that the adherence of this thin maternal remnant does little to prevent loss of fœtal blood. Personally I believe that the cord should be tied at once in order to conserve the fœtal blood-volume.

Dundee. A. E. CHISHOLM.

## WHAT'S IN THE LOAF?

SIR,—Your timely leader discloses a situation nearly incredible but so obviously in accordance with the ugly facts that further action is required.

When the Medical Research Council issued their memo on national flour last spring it was understood that it contained the specification of national wheatmeal flour which we were asked to eat. Any doubts about this were dispelled when Lord Woolton, addressing the bakers at their national conference at Leicester in June, said he had been at great trouble over the bread question but had been "advised by the most eminent scientists in the country" and mentioned the Medical Research Council by name in this connexion. Everyone understood that one of the two 85% extraction flours specified in that memo was a specification of the wheatmeal bread to be introduced by the Ministry of Food. It did not matter which; the millers were for their convenience to make one of these and then pass on to the other. No other specification was issued nor any information given by the Ministry of Food casting any doubt; we knew what national flour was to be. The specification was therefore examined and found good, especially when reports were issued by various nutritional laboratories as to the B vitamins, minerals, &c. this flour could be relied on to supply. I therefore started a campaign to popularise wheatmeal bread, explaining to patients how they would thus get a generous supply of the essential B vitamin as well as four times the anæmia-preventing iron they got from white flour. How by this means the Ministry had made a cheap protective food available. That it contained even less indigestible fibre than white and would be more digestible. I was confirmed in these views when Circular 2470 was received from the Ministry of Health in June. This was sent to me in my capacity of M.O. to the local infirmary and asked me to make the new bread available to patients and staff. This circular is so illuminating that I quote one passage in full.

"The Minister has been in consultation with the Minister of Food on this matter and he is advised that national wheatmeal flour is now available to bakers. This flour contains the greater part of the germ of the wheat, with some of the finer bran, but excludes the coarser bran. It thus contains not only most of the vitamin $B_1$, but also most of the remainder of the vitamin-B complex, as well as valuable minerals removed in producing white flour. National wheatmeal flour is therefore of high nutritional value and is particularly valuable at times when there is restriction upon the availability of other foods from which these vitamins and minerals could be obtained."

Can anyone doubt that the flour specified by the Medical Research Council was under consideration? There was no other published, or known, and the reference to the fineness of the fibre left in is itself sufficient evidence if any were needed. You now call attention to an order of the ministry regulating what national wheatmeal flour really is to be, and which was issued only two months after the consultations between the ministries on the same subject. As you explain it this order simply makes fun of what the Minister of Health was told. Or perhaps I had better say of what he informs us he was told by the Minister of Food. Instead of containing the greater part of the germ of the wheat the flour need not contain any. Instead of containing most of the $B_1$ vitamin it need not contain more than white flour from which most of it has been removed. Instead of containing most of the remainder of the B complex this will be absent as will the valuable minerals. For it may be nothing more than white flour to which some bran has been added!

So all that I have been telling patients, on the word of two ministries, has been without justification. I object to being misled at any time, but particularly on a matter of such importance to us all in war-time.

It will only be fair to the M.R.C. if I state that a letter from the council informs me that the policy of the country as regards the production of white and brown bread is decided entirely by the Ministry of Food and that they have nothing to do with this; the letter concludes (italics mine): "No doubt, IF the Medical Research Council had to give advice *without taking into consideration any other body*, they would recommend 85% extraction flour with added calcium...." Compare this situation with that at the Air Ministry and ask where we should be today if Sir Archibald Sinclair had adopted the same attitude towards his scientists, and left planes to be made in ways giving most profit to manufacturers. Because can anyone doubt that financial interests have a connexion with the change of front on wheatmeal? Or is it simply the dullness shown by the previous representative of the Ministry of Food in the House of Commons who declared there "We want no scientific stunts on the Kitchen Front"? The Ministry of Food have able men who understand nutrition at their service. Why are they not being used?

All should be grateful to you for raising such a vital though unpleasant question.

Grimsby. S. W. SWINDELLS.

## PERINÆAL SUTURE UNDER LOCAL ANÆSTHESIA

SIR,—In your annotation last week (p. 611) you rightly emphasise the value of repair of the perinæum under local anæsthesia and refer to a paper by B. Williams and to another by Neal Smith, the latter reporting its use with good results in 17 cases at Charing Cross Hospital. Thirteen years ago in your columns (*Lancet*, 1928, **1**, 1281) I described an exactly similar method even to the insertion of the needle through the skin surface and stressing, as Dr. Smith does, the importance of infiltrating the tissues immediately under the skin or mucous membrane. The only difference between Dr. Smith's method and mine, so far as I can see, is that I advised the addition of adrenaline chloride solution (1 drop of a 1 : 1000 solution to each drachm of Novocain) and pointed out that it spared the patient any pain from insertion of the needle if a swab soaked in the solution was placed for 5 minutes beforehand against the raw surface. The method as described by me has since been in routine use by the students and staff in the obstetric unit of University College, both in the hospital and on the district, and during these 13 years it must have been used in several thousand cases. The results have been so uniformly satisfactory that no one has suggested that it should be discontinued. To my knowledge the method is now routinely and successfully used in at least three other London hospitals.

University College Hospital, W.C.1. F. J. BROWNE.

## STUDENT AND SCREEN

SIR,—The comments in your issue of Nov. 8 draw attention to the neglected possibilities that lie in the film for teaching medical students. The increasing amount that has to be learnt in a limited time makes it surprising that no request for use of films has yet been made by medical students. Though academic circles in this country have hardly noticed this weapon, there are a number of good scientific films that could be more widely used in teaching—films on mathematics, physics, chemistry, biology, anatomy and physiology, and films illustrating operative technique in surgery and obstetrics. Medicine has not yet been filmed so much, though the film on malaria which you reviewed is of very high quality. There are films on subjects ranging from oxygen therapy to the treatment of war neuroses, there are health education films for children and adult audiences, and the relation of medicine to the community is illustrated in films such as the British Commercial Gas Association's excellent nutrition film "Enough to Eat," and the Ministry of Information film "Health in War."

The chief reason why a wider use has not yet been made of available films is probably ignorance either of their existence or of how to get hold of them. The Scientific Films Committee of 30, Bedford Row, W.C.1, have viewed a large number of scientific films and are continuing to do so. A list of scientific films with an independent evaluation of their merit for showing to

expert and to general audiences and for teaching purposes has been prepared. Detailed critiques of these films and their contents are also available. The S.F.C. has arranged a number of film shows at the request of various medical societies, and also shows of health films (similar to the public health show given by the London Scientific Film Society last winter) for more general audiences. It is important that films should be used widely in the health education of the public, and a start has been made with "Defeat Diphtheria" and "Breath of Danger." The committee will be glad to give information to those who wish to know more about or to arrange shows of films of medical interest.

London, W.C.1. RONALD MACKEITH.

### DISPOSAL OF STILLBORN CHILDREN

SIR,—The sequel to the story of your peripatetic correspondent, or one like it, about the fœtus in the abdomen of a man, was that the mortician rather unnecessarily reported it to the coroner. As the body had been removed some miles away from the hospital the coroner was concerned that the body should have got into his jurisdiction and did not quite know what to do about it. So he reported to the Home Office who sent one of the Big Five from Scotland Yard to see me on a Sunday morning to suggest that the mortuary keeper had been aiding and abetting the offence of concealment of birth. Of that it was shown that he was not guilty. However, the chief inspector's visit was followed by a documentary admonition to which I was able to reply that the procedure of placing a baby's body in the coffin of an adult had written authority from the Home Office, given some years before. Whereupon there was some flutter in the official dovecote. The hospital changed its procedure but the disposal of stillborn children still gives trouble.

BETA.

## Appointments

ALCOCK, WILLIAM, M.B. Sheff., B.Hy. Durh., D.P.H.: M.O.H. and school M.O. for Burton-on-Trent.
COKKINIS, A. J., M.B. Lond., F.R.C.S.: V.D. specialist at Hillingdon and West Middlesex county hospitals.
COOPER, J. D., L.R.C.P.E., L.D.S.: temp. asst. M.O. at Forest Gate Hospital, West Ham.
FERRIS, R. D., M.B. Melb., F.R.C.S.E.: deputy R.S.O. at Coventry and Warwickshire Hospital.
NELSON, MARY, L.R.C.P.I.: temp. asst. T.O. for Sheffield.
POLLEY, S. F., M.R.C.S.: R.S.O. at Rugby Hospital.
SUTTON, S. J., M.R.C.S.: temp. asst. M.O., Whipps Cross Hospital, West Ham.

*Colonial Service.*—The following appointments are announced:
BOWYER, J. H., M.B. Dubl., D.P.H., D.T.M. & H.: superscale officer (grade A), Malaya.
SHIRCORE, J. O., M.B. Edin., M.R.C.P.E.: M.O., Nyasaland.
WAKEFIELD, T. C., M.B. Edin., L.M.: superscale officer (grade B), Malaya.

## Births, Marriages and Deaths

### BIRTHS

BABINGTON.—On Nov. 12, at Leicester, the wife of Major G. C. Babington, R.A.M.C.—a son.
CLARKSON.—On Nov. 11, at Witney, Oxon, the wife of Major Patrick Wensley Clarkson, R.A.M.C.—a son.
HAGENBACH.—On Nov. 8, at Bath, the wife of Dr. Charles Hagenbach—a daughter.
HAYWARD-BUTT.—On Nov. 11, at Crail, Fife, the wife of Surgeon-Lieutenant Peter Hayward-Butt, R.N.—a son.
KEKWICK.—On Nov. 13, at Mursley, Bletchley, Bucks, the wife of Major Alan Kekwick, R.A.M.C.—a son.
LEISHMAN.—On Nov. 14, 1941, at Alresford, Hants, the wife of Dr. Hugh Leishman—a son.

### MARRIAGES

WILKIE—DUFFY.—On Nov. 29, at Upminster, Essex, Duncan Richard Primrose Wilkie, M.R.C.S., captain R.A.M.C., to Mary Duffy, S.R.N.

### DEATHS

GOLLAND.—On Nov. 14, Alfred Golland, M.R.C.S., of Holly Mount, Bosbury.
GRAHAM.—On Nov. 11, at Edinburgh, Frederick Maurice Graham, M.D. Durh., F.R.C.S., chevalier de la Légion d'Honneur.
MORRIS.—On Nov. 11, at Bognor Regis, Henry Cecil Low Morris, M.D. Brux., M.R.C.S.
WRAITH.—On Nov. 13, Oswald Samuel Wraith, M.D., F.R.C.S.E., of Bournemouth, aged 83.

In a recent casualty list W. S./Captain L. Maclean, R.A.M.C., was posted as a prisoner of war.

## Medical News

### Royal College of Surgeons of England

At a meeting of the council held on Nov. 13, with Sir Alfred Webb-Johnson, the president, in the chair, the following were re-elected members of the court of examiners for one year from Dec. 11: Mr. R. Milne, Mr. R. Davies-Colley, Mr. G. T. Mullally, Mr. V. Z. Cope, Mr. C. E. Shattock and Mr. E. W. Riches.

Diplomas of membership and public health were granted (with the exception of F.-X. Darne, J. D. C. Gowans, D. K. Sambrook, A. L. H. Smith, and Glenys Wade) to the candidates named in the report of the comitia of the Royal College of Physicians in THE LANCET of Nov. 8, p. 585. Licences in dental surgery were granted to the following:—

Denis Abraham, J. E. L. Armitage, Barbara M. Barnes, Rolf Bergmann, R. D. Bookless, N. A. Bostock, J. A. Boyd, B. G. Brown, A. E. Cadman, M. F. Caton, Philip Cohen, R. F. Cutmore, C. I. De Silva, A. W. Donald, John Dunnett, W. J. Ford, J. H. Forrester, R. M. Gillies, A. P. Gimson, A. E. G. Goodfellow, F. L. Hall, T. J. Hancock, M. H. Holmes, Eric Horne, J. P. Howes, A. V. Hurst, M. A. Kettle, D. E. Laurie, J. F. K. Leggett, T. A. Lock, John Morris-Wilson, Esther M. Myers, A. B. Nahaboo, D. A. T. Payne, W. L. Renouf, Gwendolen M. Rodgers, Allan Ross, D. F. Soul, Pauline Stacey, Henry Stooke, R. V. Tait, J. R. H. Williams, J. T. Willmott, H. J. W. Wilmshurst and F. M. Wood.

### Society of Apothecaries of London

The following candidates, having completed the final examination, have been granted the diploma of the society entitling them to practise medicine, surgery and midwifery: G. M. Pearson, Guy's; J. S. Taylor, Leeds; H. A. Worthy, Sheff.; and S. S. Zoha, Osmania and N.E. Lond. Post.-Grad. Hosp.

### University of Wales

At recent examinations for the degrees of M.B., B.Ch. A. A. Edwards satisfied the examiners in the subject of medicine.

### University of Sheffield

The following appointments have been made: medical tutors, Dr. H. P. Brody and Dr. J. Pemberton; surgical tutors, Mr. A. W. Fawcett and Mr. H. Blacow Yates; obstetrical tutor, Dr. W. J. McCord; hon. lecturer in applied anatomy, Mr. J. T. Chesterman; and research assistant to the department of pathology and to the cancer research laboratories: Dr. M. J. Pivawer.

The following external examiners were appointed in the faculty of medicine: anatomy, Prof. R. D. Lockhart; physiology, Prof. R. J. S. McDowall; medicine and therapeutics, Prof. L. G. Parsons; pathology and bacteriology, Prof. S. L. Baker; obstetrics and gynæcology, Prof. A. L. Robinson; forensic medicine, Prof. Sydney Smith; pharmacology, Prof. W. J. Dilling; and public health, Dr. J. A. Charles.

The following were appointed representatives on the committee of management of Sheffield Hospitals Council: The junior pro-chancellor, the vice-chancellor, Mr. H. J. W. Marsh, Prof. H. N. Green, M.D., and Prof. E. J. Wayne, F.R.C.P.

### Royal Society of Medicine

On Monday, Nov. 24, at 2 P.M., Surgeon Lieut.-Commander John Bunyan, L.D.S., will read a paper to the section of odontology on the treatment of mouth infections with particular reference to the use of electrolytic sodium hypochlorite. On Nov. 27, at 2.30 P.M., at the section of urology Mr. Clifford Morson, Mr. Charles Wells and Mr. Hugh Barry will open a discussion on rupture of the urethra and its treatment. On Nov. 28, at 2.30 P.M., the section of disease in children will discuss the effects of war-time rationing on child health, and the openers will be Miss E. M. Widdowson, Ph.D., Dr. Dagmar Wilson and Dr. W. W. Payne. At 3 P.M., on the same day, at the section of epidemiology and state medicine, Dr. Melville Mackenzie will read a paper on the control of louse-borne typhus and Dr. G. M. Findlay and Prof. P. A. Buxton will also speak.

### Vitamins for Babies

From Dec. 8, the Ministry of Food in coöperation with the Ministry of Health will distribute fruit juices and a cod-liver oil compound to all children born after Jan. 1, 1940. The first issue of fruit will be blackcurrant syrup or puree but later concentrated orange juice from America will be available. The ration will ensure an adequate intake of vitamins C, A and D to some 1,360,000 children. Distribution will be made through maternity and child-welfare centres and food offices.

### Medical Society of London

A meeting of this society will be held at 11, Chandos Street, W.1, on Nov. 24 at 3.30 P.M., when Dr. John Parkinson will read a paper on heart attacks, Mr. V. E. Negus on congenital shortening of the œsophagus, and Mr. Guy Blackburn on regional ileitis.

### Royal Medico-Psychological Association

A meeting of this association will be held on Nov. 26, at 11, Chandos Street, London, W.1, at 2.15 P.M., when Dr. E. Lilian Hutton will read a paper on the investigation of personality in patients treated by prefrontal leucotomy.

### Biochemical Society

A meeting of this society will be held at the Courtauld Institute, Middlesex Hospital, London, W.1, on Saturday, Nov. 29, at 11 A.M., when Dr. G. M. Findlay will open a discussion on the modes of action of chemotherapeutic agents.

### Medico-Legal Society

A meeting of this society will be held at 26, Portland Place, London, W.1, on Thursday, Nov. 27, at 4 P.M., when Dr. H. Neville Stafford will read a paper on the coroner and civilian war deaths.

### Socialist Medical Association

At a meeting of this society on Saturday, Nov. 22, at 12, Great Newport Street, London, W.C.2, at 2.30 P.M., Sir Albert Howard and Mr. Frederick Ridley, F.R.C.S., will speak on agriculture and health.

### War Wounds Committee in Scotland

The Medical Research Council has set up in Scotland a subcommittee of their war wounds committee. The members are Prof. J. R. Learmonth (chairman), Dr. A. B. Wallace (secretary), Prof. J. S. Young, Prof. R. C. Alexander, Prof. D. F. Cappell, Prof. C. F. W. Illingworth, Prof. C. H. Browning, Dr. D. P. Cuthbertson, Sir John Fraser, Prof. T. J. Mackie, Mr. C. P. Stewart, Ph.D. and Dr. J. M. Johnston.

### Domestic Staff in Hospitals

In recognition of the national importance of domestic work in hospitals the Minister of Health has decided to issue a badge to all those employed on domestic work in hospitals, who give at least 96 hours regular service each month. Women who are whole-time hospital helpers on registration will not be called for interview.

### Calls to the Bar

On Nov. 17 the following were called to the bar: Lieut.-Colonel Ralph Brooke, F.R.C.S., R.A.M.C. (Inner Temple); Dr. F. H. Blackburn and Mr. E. A. Butterworth, F.R.C.S. (Middle Temple); and Dr. A. P. Cogswell (Gray's Inn).

### Control of Scabies

The Minister of Health has issued a new regulation giving medical officers of health authority to inspect premises in which verminous people have been accommodated and to examine and treat other people on those premises. They may also order the cleansing or destruction of articles on the premises.

### International Hospital Association

At 2 P.M. on Nov. 25 at B.M.A. House, Tavistock Square, W.C.1, the United Kingdom council of this association will hold a conference to discuss the position of hospitals in the post-war world. Prof. A. T. Jurasz, dean of the Polish medical faculty in the University of Edinburgh, will read a paper on the international position of hospitals after victory and the coming of peace. Representatives of 54 countries have been invited to attend, and the Minister of Health will be present. Admission will be by special ticket only, and further information may be obtained from the hon. secretary, 47, Bloomsbury Square, London, W.C.1.

### Anglo-Soviet Medical Committee

The aims of this committee are to form a liaison between the medical professions of Great Britain and the U.S.S.R., to exchange the latest clinical and scientific knowledge, to facilitate visits of medical specialists between the two countries, and to give specialist advice on medical aid to the U.S.S.R. It is proposed to make the minimum annual subscription for associate members 5*s*. A bulletin on the committee's work will be issued from time to time and a general meeting will be held early in the new year. Those who wish to become associate members should write to the hon. secretary of the committee, 1, Wimpole Street, London, W.1.

## Notes, Comments and Abstracts

### HOME VISITING OF DEFAULTING VENEREAL-DISEASE PATIENTS

J. L. BURN, M.D. DURH., B.HY., D.P.H.
MEDICAL OFFICER OF HEALTH, CITY OF SALFORD

A NOTE of a year's working of a scheme of home visiting of defaulting female patients who had attended a venereal-diseases clinic may be worthy of record. Only women and children were followed up; these consisted of female patients who had defaulted in attendance at the venereal-diseases clinic of the county borough of Barnsley and some special cases referred thereto. All the defaulters (some of whom had not been seen for some years) had received several invitations by letter to attend, and up to the time of the visit all these letter-invitations had proved ineffective. It is considered that the number who would have returned to the clinic without a visit would have been negligible.

The home visiting was carried out by a health visitor who also acted as a part-time nurse in the venereal-disease clinic, and part-time health visitor in the maternity and child-welfare service. An advantage was that the visitor was not "known" to patients or public as a venereal-disease visitor. Additionally, her position enabled close liaison to be maintained between other health visitors and medical officers of the maternity and child-welfare and school medical services. The visiting—which was done with the aid of a car—occupied time equivalent to one session only per week; thus, for the year's working, the number of sessions occupied in home visiting was under 50.

In all, 163 persons were visited. The medical diagnoses on the case-sheets of the persons visited were: syphilis or ? syphilis, 105; gonorrhœa or ? gonorrhœa, 38; non-venereal disease, 20. The total number of visits paid was 305: 92 persons were visited once; 28 persons twice; 23 persons three times; 15 persons four times; 3 persons five times; 1 person six times; and 1 person seven times. Of the 163 persons, it was found that 26 had removed and 3 had died, leaving a net total of 134. Of these, over a third (i.e. 50, or 37% of the total) attended regularly, while another 16 attended more or less regularly.

On visiting several clinics throughout this country, I was impressed by the fact that some of the most dangerous types of patients from an infective point of view are young people who default after a few attendances—this despite the fact that the patients were handled with the greatest tact and efficiency. In each case, verbal promise had been obtained to continue attendance until cured. It is always easy to elicit promises in the clinic. Follow-up letters had proved of no value.

In addition to the problem of defaulting, the problem of untraced contacts is serious—only 10% of the wives or partners of infected patients on an average were traced. These facts are full of danger to the public health, and make consideration of the help which home visiting can give more urgent.

Figures quoted in the excellent booklet of the British Social Hygiene Council, "Notes on Social Service in the Treatment Centre," are very striking. At St. Mary's Hospital, Paddington, the proportion of defaulters in the total number of patients is now as low as 6%, owing in large measure to the work of the almoner, described in Miss Dorothy Manchée's book "Social Service in the Clinic for Venereal Diseases" (London, 1938). At Guy's Hospital, the percentage of defaulters who were induced to return rose in six years from 46% to 80%. At the corporation V.D. department in Edinburgh, among the women and children patients, 9 out of every 10 defaulters were persuaded by the nurse's visits to return and continue treatment. In 1921–22, before the appointment of a nurse-almoner, the defaulter rate was 54%; in 1937 it was 8·5%.

The appointment of a fully trained almoner of the right personality is undoubtedly ideal, but many clinics are too small for the whole-time employment of an almoner, and there are not sufficient trained almoners to go round. The task of persuading committees to make

such an appointment is not easy, and it was with this in mind that I deemed it wise to proceed cautiously and utilise the services of a member of the health-visiting staff in the scheme described. When the good results of such visiting are proved it will be simpler to persuade an authority to go ahead with the appointment of an almoner, or to join a group of authorities and thus to justify a whole-time appointment. In dealing with so difficult a disease as venereal disease, which has social, psychological and moral complications and legal snags, it is essential to select a nurse of the right personality, discretion and power of persuading patients. In nursing staffs of large health departments there is sure to be one or more who fulfils these conditions, and thereby a start can be made in this valuable work.

### VALUE OF HOME VISITING

It is claimed that the results of this small scheme are sufficient justification for the venture and the expense involved. To get over a third of the defaulters to attend regularly is of decided value, but the results cannot be assessed merely by statistics. Two individual cases are worthy of description.

CASE 1.—A girl, aged 16, with acute gonorrhœa. This acutely infectious case, living under bad home conditions, defaulted before completing treatment. The visitor got to know her patient, and the mother's opposition melted before a simple explanation of the function of a special treatment centre. The patient was persuaded to attend. Again she defaulted. Further visits resulted in regular attendance, and she was finally discharged cured. In this case, the girl was put in touch with a girls' club, and it is believed that much social as well as physical good to her future life has ensued from the intervention of the visitor. It is reasonable to assume that the possible consequences of this girl's defaulting would certainly have been a danger to herself, and probably to others.

CASE 2.—A woman, aged 27, with congenital syphilis. This patient suffered from interstitial keratitis and iridocyclitis. She consented to visit the clinic only after many visits had been paid, and the visitor arranged to accompany her to the clinic. Subsequently, this patient defaulted, but after small personal problems had been dealt with treatment was continued more or less regularly. Her eye condition dramatically improved. This would not have been achieved if ordinary clinic methods of follow-up letters had been employed to secure further attendance.

Only by means of visiting can the real reason of defaulting be discovered. These patients are human—all too human. There are numerous obstacles to attendance, some minor and absurd, but they are often easily overcome by right handling. Weariness in attending, the wishful thinking whereby patients believe attendance unnecessary on the cessation of an obvious discharge, quarrels on the subject between husband and wife, ill health, the glib promise to attend given to the doctor in the clinic, the terror of discovery or losing a job, the threat to happiness, the guilty conscience or innocent shame—these factors, of enormous importance, show that cure of venereal disease is not entirely a medical problem.

Home visiting was worth while in the case of mothers who had been treated antenatally Such patients are prone to default. The birth of an apparently healthy baby convinces the mother that there is no further need to attend, while the added care of the baby renders attendance difficult. In several cases the private practitioner was said to have informed them they that did not require to attend.

Cases visited with the least success were those who live in "houses let in lodgings" and who frequently move from town to town. Several such women suffering from acute gonorrhœa (living in the same house and having been infected by the same man) attended for a short time, defaulted, and when they were visited it is found they have moved on, leaving no address. In one family where the children were congenitally infected the reason for defaulting given was that the journey to the clinic was too long. This reason would never have been given in response to a letter, but could only be elicited on visiting the home. In this case arrangements were made for the treatment to be given at a nearby school clinic.

In several cases it was discovered that the times at which the clinic was opened were unsuitable. It is of obvious importance for the staff in charge of a clinic to be acquainted with these deterrents, yet I do not see how the staff can realise all the difficulties unless the facts which are gained from home visiting are known to them. War-time difficulties of shift work, blackout, transport difficulties and increased female employment aggravate the obstacles to attendance, and it is more than ever important that these factors should be brought to light so that the authorities can as far as possible make the clinics suit the patients, and make minor but nevertheless important improvements in clinic services.

In only 2 cases were there definite refusals to discuss the question of attendance at V.D. clinics. In 20 of the 134 the patients gave a definite refusal to attend, and this refusal was accepted. Medical officers have the consolation of knowing that, at any rate, the patients have been warned, and that every expedient has been used to ensure attendance. No attempt was made—nor was any necessary—to browbeat the patients into attending. In many cases, simple methods of explanation, kindness and encouragement were all that were required to dispel ignorance and fear and secure coöperation.

No attempt was made to solve the thornier problem of visiting defaulting male patients or contacts. I know of no record of this work being done at all in this country. On a pre-war visit to a Paris clinic I admired the ease and objectivity with which this work was done.

The confidential nature of venereal disease treatment was preserved. No legal difficulties were encountered. The scheme was economical—a useful point in persuading committees—the cost of the time of the nurse in visiting would not amount to more than £25 throughout the year. This expense is small in view of the results obtained in the 2 cases quoted above, apart from the general fact that some attendance of nearly half of the patients who had defaulted was secured, while the attendance of over a third of chronic defaulters to the end of treatment and tests of cure was ensured.

Very few venereal-disease clinics in this country use a home visitor to induce defaulters to complete treatment or to trace and treat contacts, yet I consider that the home visitor is an essential member of the team necessary to achieve greater success in this difficult work.

I acknowledge the ever-ready help and encouragement given by officers of the British Social Hygiene Council. Any success which the scheme had is due to the personal effort of Miss Hilda E. Myers of the Barnsley health department.

## REEVE TO THE L.C.C.

THE mental hospitals committee of the council have always been farmers in a small way, for it was considered wise that patients at the mental hospitals of the county should where possible have a chance of doing healthful work in the open air, and farms were attached to several institutions. Since the outbreak of the war the farmland of the council has been nearly doubled—today they farm over 5000 acres—and last July they asked the committee to undertake the general control of their scattered plots. It therefore fell to the mental hospitals committee to present the report of the yield of the council's lands up to the end of March, 1941, though this was before they took over. The committee explain that the drastic rationing of foodstuffs caused a fall in the number of eggs produced (359,000 in 1941 against 556,000 in 1939). Outbreaks of foot-and-mouth disease reduced the number of cows kept and the milk production fell from 650,000 gallons in 1939 to 543,000 gallons in 1941. Next year, under the new scheme of coördination the committee hope to increase the production of vegetables, potatoes and animal foodstuffs by as much as 60%, 250% and 375% over their pre-war levels of 1200 tons, 1000 tons and 1400 tons respectively. If there should be a shortage of supplies the products of these farms will form a valuable pool of foodstuffs on which the claims of hospitals will be given priority.

CORRIGENDA.—The Minister of Health's request in circular 2498 (see *Lancet*, Nov. 8, p. 571) that tuberculosis notifications should reach him promptly was addressed to county councils and county borough councils. The circular was sent to the other bodies mentioned for information only.—In the summary of Major Palmer's article of Nov. 8 (p. 563) for "antitetanic serum" read "tetanus toxoid."